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=> d his

     (FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004
L1       1253188 S KINASE?
L2        182160 S HISTIDINE
L3          4732 S L1(A)L2
L4       6785689 S CLON? OR EXPRESS? OR RECOMBINANT
L5        249014 S STAPHYLOCOCCUS (A)AUREUS
L6           163 S L3 AND L5
L7           102 S L4 AND L6
L8            58 DUP REM L7 (44 DUPLICATES REMOVED)
                 E WALLIS N G/AU
L9           119 S E3
                 E SHILLING L K/AU
L10           93 S E3-E9
                 E MOONEY J L/AU
L11           63 S E3
                 E DEBOUCK C/AU
L12          416 S E3
L13          612 S E3-E8
                 E ZHONG Y Y/AU
L14           40 S E3
                 E JAWORSKI D D/AU
L15          276 S E3-E10
                 E WANG M/AU
L16         6684 S E3
                 E THROUP J P/AU
L17          115 S E3-E7
L18         7894 S L8 OR L9 OR L10 OR L11 OR L13 OR L14 OR L15 OR L16 OR L
L19           72 S L6 AND L18
L20           59 DUP REM L19 (13 DUPLICATES REMOVED)
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FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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FILE 'MEDLINE' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'EMBASE' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'BIOSIS' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'BIOTECHDS' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'SCISEARCH' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'HCAPLUS' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'NTIS' ENTERED AT 12:00:12 ON 12 NOV 2004

FILE 'LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004


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=> s kinase?
L1     1253188 KINASE?

=> s histidine
L2      182160 HISTIDINE

=> s l1(a)l2
L3        4732 L1(A) L2

=> s clon? or express? or recombinant
   4 FILES SEARCHED...
L4     6785689 CLON? OR EXPRESS? OR RECOMBINANT

=> s staphylococcus (a)aureus
L5      249014 STAPHYLOCOCCUS (A) AUREUS

=> s l3 and l5
L6         163 L3 AND L5

=> s l4 and l6
L7         102 L4 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8           58 DUP REM L7 (44 DUPLICATES REMOVED)

=> d 1-58 ibib ab

L8   ANSWER 1 OF 58  SCISEARCH  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
ACCESSION NUMBER:    2004:517041  SCISEARCH
THE GENUINE ARTICLE: 824CT
TITLE:               Identification of a novel two-component system in
                     Streptococcus gordonii V288 involved in biofilm formation
AUTHOR:              Zhang Y S; Lei Y; Khammanivong A; Herzberg M C (Reprint)
CORPORATE SOURCE:    Univ Minnesota, Dept Oral Sci, 17-164 Moos Tower, 515
```

Delaware St SE, Minneapolis, MN 55455 USA (Reprint); Univ Minnesota, Dept Oral Sci, Minneapolis, MN 55455 USA; Univ Minnesota, Mucosal & Vaccine Res Ctr, Minneapolis, MN 55455 USA; Univ Minnesota, Sch Dent, Dept Oral Sci, Minneapolis, MN 55455 USA

COUNTRY OF AUTHOR: USA

SOURCE: INFECTION AND IMMUNITY, (JUN 2004) Vol. 72, No. 6, pp. 3489-3494.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Streptococcus gordonii is a pioneer colonizer of the teeth, contributing to the initiation of the oral biofilm called dental plaque. To identify genes that may be important in biofilm formation, a plasmid integration library of S. gordonii V288 was used. After screening for in vitro biofilm formation on polystyrene, a putative biofilm-defective mutant was isolated. In this mutant, pAK36 was inserted into a locus encoding a novel two-component system (bfr [biofilm formation related]) with two cotranscribed genes that form an operon. bfrA encodes a putative response regulator, while bfrB encodes a receptor **histidine kinase**. The bfr mutant and wild-type strain V288 showed similar growth rates in Todd-Hewitt broth (THB). A bfr-cat fusion strain was constructed. During growth in THB, the reporter activity (chloramphenicol acetyltransferase) was first detected in mid-log phase and reached a maximum in stationary phase, suggesting that transcription of bfr was growth stage dependent. After being harvested from THB, the bfr mutant adhered less effectively than did wild-type strain V288 to saliva-coated hydroxyapatite (sHA). To simulate pioneer colonization of teeth, S. gordonii V288 was incubated with sHA for 4 h in THB with 10% saliva to develop biofilms. RNA was isolated, and **expression** of bfrAB was estimated. In comparison to that of cells grown in suspension (free-growing cells), bfr mRNA **expression** by sessile cells on sHA was 1.8-fold greater and that by surrounding planktonic cells was 3.5-fold greater. Therefore, bfrAB is a novel two-component system regulated in association with S. gordonii biofilm formation in vitro.

L8 ANSWER 2 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:498290 SCISEARCH
THE GENUINE ARTICLE: 822TE

TITLE: Differential gene **expression** in response to hydrogen peroxide and the putative PerR regulon of Synechocystis sp strain PCC 6803

AUTHOR: Li H; Singh A K; McIntyre L M; Sherman L A (Reprint)
CORPORATE SOURCE: Purdue Univ, Dept Biol Sci, W Lafayette, IN 47907 USA (Reprint); Purdue Univ, Dept Agron, W Lafayette, IN 47907 USA
COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BACTERIOLOGY, (JUN 2004) Vol. 186, No. 11, pp. 3331-3345.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0021-9193.

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 75

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We utilized a full genome cDNA microarray to identify the genes that comprise the peroxide stimulon in the cyanobacterium Synechocystis sp. strain PCC 6803. We determined that a gene (slr1738) encoding a protein

similar to PerR in Bacillus subtilis was induced by peroxide. We constructed a PerR knockout strain and used it to help identify components of the PerR regulon, and we found that the regulatory properties were consistent with the hypothesis that PerR functions as a repressor. This effort was guided by finding putative PerR boxes in positions upstream of specific genes and by careful statistical analysis. PerR and sll1621 (ahpC), which codes for a peroxiredoxin, share a divergent promoter that is regulated by PerR. We found that isiA, encoding a Chl protein that is induced under low-iron conditions, was strongly induced by a short-term peroxide stress. Other genes that were strongly induced by peroxide included sigD, sigB, and genes encoding peroxiredoxins and Dsb-like proteins that have not been studied yet in this strain. A gene (slr1894) that encoded a protein similar to MrgA in B. subtilis was upregulated by peroxide, and a strain containing an mrgA knockout mutation was highly sensitive to peroxide. A number of genes were downregulated, including key genes in the chlorophyll biosynthesis pathway and numerous regulatory genes, including those encoding **histidine kinases**. We used PerR mutants and a thioredoxin mutant (TrxA1) to study differential **expression** in response to peroxide and determined that neither PerR nor TrxA1 is essential for the peroxide protective response.

L8 ANSWER 3 OF 58 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004166238 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15060046
TITLE: Characterization of virulence factor regulation by SrrAB, a two-component system in **Staphylococcus aureus**.
AUTHOR: Pragman Alexa A; Yarwood Jeremy M; Tripp Timothy J; Schlievert Patrick M
CORPORATE SOURCE: Department of Microbiology, University of Minnesota Medical School, Minneapolis, Minnesota 55455, USA.
CONTRACT NUMBER: T32 AI 07421 (NIAID)
SOURCE: Journal of bacteriology, (2004 Apr) 186 (8) 2430-8. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF260326
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040403
Last Updated on STN: 20040525
Entered Medline: 20040524

AB Workers in our laboratory have previously identified the staphylococcal respiratory response AB (SrrAB), a **Staphylococcus aureus** two-component system that acts in the global regulation of virulence factors. This system down-regulates production of agr RNAIII, protein A, and toxic shock syndrome toxin 1 (TSST-1), particularly under low-oxygen conditions. In this study we investigated the localization and membrane orientation of SrrA and SrrB, transcription of the srrAB operon, the DNA-binding properties of SrrA, and the effect of SrrAB **expression** on S. aureus virulence. We found that SrrA is localized to the S. aureus cytoplasm, while SrrB is localized to the membrane and is properly oriented to function as a **histidine kinase**. srrAB has one transcriptional start site which results in either an srrA transcript or a full-length srrAB transcript; srrB must be cotranscribed with srrA. Gel shift assays of the agr P2, agr P3, protein A (spa), TSST-1 (tst), and srr promoters revealed SrrA binding at each of these promoters. Analysis of SrrAB-overexpressing strains by using the rabbit model of bacterial endocarditis demonstrated that overexpression of SrrAB decreased the virulence of the organisms compared to the virulence of isogenic strains that do not overexpress SrrAB. We concluded that SrrAB is properly localized and oriented to function as a two-component system. Overexpression of SrrAB, which represses agr RNAIII, TSST-1, and protein A

in vitro, decreases virulence in the rabbit endocarditis model. Repression of these virulence factors is likely due to a direct interaction between SrrA and the agr, tst, and spa promoters.

L8 ANSWER 4 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:271816 SCISEARCH
THE GENUINE ARTICLE: 802HO
TITLE: pbp2229-mediated nisin resistance mechanism in Listeria monocytogenes confers cross-protection to class IIa bacteriocins and affects virulence gene **expression**
AUTHOR: Gravesen A (Reprint); Kallipolitis B; Holmstrom K; Hoiby P E; Ramnath M; Knochel S
CORPORATE SOURCE: Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark (Reprint); Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, DK-1958 Frederiksberg C, Denmark; Univ So Denmark, Dept Biochem & Mol Biol, DK-5230 Odense, Denmark; Bioneer A S, Dept Mol Characterizat, DK-2970 Horsholm, Denmark; Univ Stellenbosch, Dept Biochem, ZA-7602 Matieland, South Africa
COUNTRY OF AUTHOR: Denmark; South Africa
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (MAR 2004) Vol. 70, No. 3, pp. 1669-1679.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0099-2240.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 50

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB It was previously shown that enhanced nisin resistance in some mutants was associated with increased **expression** of three genes, pbp2229, hpk1021, and Imo2487, encoding a penicillin-binding protein, a **histidine kinase** and a protein of unknown function, respectively. In the present work, we determined the direct role of the three genes in nisin resistance. Interruption of pbp2229 and hpk1021 eliminated the nisin resistance phenotype. Interruption of hpk1021 additionally abolished the increase in pbp2229 **expression**. The results indicate that this nisin resistance mechanism is caused directly by the increase in pbp2229 **expression**, which in turn is brought about by the increase in hpk1021 **expression**. We also found a degree of cross-protection between nisin and class IIa bacteriocins and investigated possible mechanisms. The **expression** of virulence genes in one nisin-resistant mutant and two class IIa bacteriocin-resistant mutants of the same wild-type strain was analyzed, and each mutant consistently showed either an increase or a decrease in the **expression** of virulence genes (prfA-regulated as well as prfA-independent genes). Although the changes mostly were moderate, the consistency indicates that a mutant-specific change in virulence may occur concomitantly with bacteriocin resistance development.

L8 ANSWER 5 OF 58 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004212976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15109784
TITLE: Regulation of virulence determinants in **Staphylococcus aureus**: complexity and applications.
AUTHOR: Bronner Stephane; Monteil Henri; Prevost Gilles
CORPORATE SOURCE: Institut de Bacteriologie, Faculte de Medecine, Universite Louis Pasteur - Hopitaux, Universitaires de Strasbourg, 3, rue Koeberle, F-67000 Strasbourg, France.
SOURCE: FEMS microbiology reviews, (2004 May) 28 (2) 183-200. Ref:

114
Journal code: 8902526. ISSN: 0168-6445.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040428
Last Updated on STN: 20040703
Entered Medline: 20040702

AB The virulence of **Staphylococcus aureus** is essentially determined by cell wall associated proteins and secreted toxins that are regulated and **expressed** according to growth phases and/or growth conditions. Gene **expression** is regulated by specific and sensitive mechanisms, most of which act at the transcriptional level. Regulatory factors constitute numerous complex networks, driving specific interactions with target gene promoters. These factors are largely regulated by two-component regulatory systems, such as the agr, saeRS, srrAB, arlSR and lytRS systems. These systems are sensitive to environmental signals and consist of a sensor **histidine kinase** and a response regulator protein. DNA-binding proteins, such as SarA and the recently identified SarA homologues (SarR, Rot, SarS, SarT, SarU), also regulate virulence factor **expression**. These homologues might be intermediates in the regulatory networks. The multiple pathways generated by these factors allow the bacterium to adapt to environmental conditions rapidly and specifically, and to develop infection. Precise knowledge of these regulatory mechanisms and how they control virulence factor **expression** would open up new perspectives for antimicrobial chemotherapy using key inhibitors of these systems.

L8 ANSWER 6 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:139965 SCISEARCH
THE GENUINE ARTICLE: 769FL
TITLE: Regulation of virulence determinants in vitro and in vivo in **Staphylococcus aureus**
AUTHOR: Cheung A L (Reprint); Bayer A S; Zhang G Y; Gresham H; Xiong Y Q
CORPORATE SOURCE: Dartmouth Coll Sch Med, Dept Microbiol, Hanover, NH 03755 USA (Reprint); Univ Calif Los Angeles, Harbor Med Ctr, Res & Educ Inst, Torrance, CA 90502 USA; Univ Calif Los Angeles, Sch Med, Los Angeles, CA 90024 USA; Natl Jewish Med & Res Ctr, Integrated Dept Immunol, Denver, CO 80206 USA; Univ New Mexico, Sch Med, Dept Microbiol & Mol Genet, Albuquerque, NM 87131 USA
COUNTRY OF AUTHOR: USA
SOURCE: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (15 JAN 2004) Vol. 40, No. 1, pp. 1-9.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0928-8244.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 53
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Staphylococcus aureus** is an opportunistic pathogen. In response to changing host environments, this bacterium has the capability to switch on selective sets of genes to enhance its chances for survival. This switching process is precisely controlled by global regulatory elements. There are two major groups of global regulatory elements in S. aureus, including two-component regulatory systems (TCRSs)

and the SarA protein family. Presumably, the sensor proteins of the 16 TCRSs in S. aureus provide external sensing, while the response regulators, in conjunction with alternative transcription factors and the SarA protein family, function as effectors within the intricate regulatory network to respond to environmental stimuli. Sequence alignment and structural data indicate that the SarA protein family could be subdivided into three subfamilies: (1) single-domain proteins; (2) double-domain proteins; and (3) proteins homologous to the MarR. protein family. Recent data using reporter gene fusions in animal models, have confirmed distinct **expression** profiles of selected regulatory and target genes in vitro vs. in vivo.

L8 ANSWER 7 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00275 BIOTECHDS
TITLE: New isolated nucleic acid encoding a peptide that kills both wild type pneumococci and a strain of Pneumococcus that is autolysin deficient, useful for treating or preventing bacterial infections or inflammations; **recombinant** protein production for use in disease therapy and drug screening
AUTHOR: NOVAK R; TUOMANEN E I
PATENT ASSIGNEE: ST JUDE CHILDREN'S RES HOSPITAL
PATENT INFO: US 6630583 7 Oct 2003
APPLICATION INFO: US 2000-493940 28 Jan 2000
PRIORITY INFO: US 2000-493940 28 Jan 2000; US 1998-84399 6 May 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-810553 [76]
AB DERWENT ABSTRACT:

NOVELTY - A new isolated nucleic acid (I) encoding a peptide comprises: the amino acid sequence selected from an amino acid sequence having 25 amino acids (P1) or (P1) with a conservative amino acid substitution; or 7-100 amino acids comprising three contiguous amino acids from (P1), where the peptide kills both wild type pneumococci, and a strain of Pneumococcus that is autolysin deficient.

WIDER DISCLOSURE - Also disclosed are: (1) an antibody against any of the proteins or peptides of the invention; (2) a pharmaceutical composition comprising one or more of the peptides and a pharmaceutical carrier; (3) a method of treating or preventing bacterial infections or inflammations; (4) a method for identifying peptides or agents capable of killing and/or inhibiting the growth of a strain of bacteria; (5) a method of identifying a cell that contains a mutation in a **histidine kinase** gene, in a response regulator gene or in a component of a gene for the ABC transporter system; (6) a peptide that acts synergistically with antibiotics that are active against bacterial cell walls; (7) a method of producing a peptide by chemical synthesis or **recombinant** technology; (8) a method of testing putative peptide antibiotics to identify new agents useful in preventing bacterial proliferation and/or causing cell death or lysis; (9) a method of designing putative peptide antibiotics through altering the amino acid and/or nucleic acid sequences of a peptide encoded by an open reading frame; and (10) a method of detecting and/or identifying penicillin or vancomycin tolerant bacterial strains.

BIOTECHNOLOGY - Preferred Peptide: The peptide encoded by the nucleic acid consist of 12-50 amino acids, preferably 25-35 amino acids or 17-35 amino acids.

ACTIVITY - Antibacterial; Antiinflammatory; Gynecological; Antitubercular; Tuberculostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - (I) is useful in preventing or treating disease caused by a bacterium, e.g. **Staphylococcus aureus**, Acietobactor, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, which all causes blood poisoning, Mycobacterium tuberculosis which causes

tuberculosis, Shigella dysenteria which causes dysentery, Neisseria gonorrhoeae which causes gonorrhoea and Streptococcus pneumoniae which causes blood poisoning, middle ear infections, pneumonia or meningitis in humans. The peptides can be employed as a preservative or as part of a composition used as a preservative. It can also be used as a laboratory tool, e.g. in conjunction with one or more bacteria; drug selection markers.

ADMINISTRATION - The composition comprising the peptides can be administered topically, parenterally (intravenous injection, intra-arteriole, intramuscular, intradermal, subcutaneous, intraperitoneal, intraventricular or intracranial), transmucosally (orally, nasally or rectally) or transdermally. No dosage given.

EXAMPLE - Genome analysis was performed using FASTA, TFASTA, BLAST and BLASTN programs. A nucleotide sequence having 75 bp or amino acid sequence having 25 amino acids were used to search existing public databases containing the multiple bacterial genomes. Homologues were found in Methanococcus, Haemophilus, Archlaeoglobus, Borrelia and Synechocystis. Cell growth curves were performed in the presence or absence of the test reagents. Samples were prepared as follows: 1 ml of Pneumococcus culture was placed into 10 ml of prewarmed Semisynthetic (C+Y) medium. The optical density (OD) of the bacteria was monitored at 620 nm until an OD of approximately 0.1 was reached. At this point the test reagents were administered to the samples. The cells were cultured for up to 11 hours at 37 degrees Centigrade and the OD at 620 nm was monitored every hour. A decrease in OD620 is indicative of cell lysis, an increase is indicative of bacterial growth. No change in optical density indicates bacterial growth. The open reading frames in a gene cluster encoding an ABC transporter and a two component His-Asp phosphorelay pathway of Streptococcus pneumoniae were examined in pursuit of a putative peptide that might be involved in autolysis. A short open reading frame was located between ORFW1-W3 and RR/HK at approximately position 6500. This short open reading frame (P) has a nucleotide sequence having 75 bp and encodes a peptide having an amino acid sequence with 25 amino acids. The peptide having 25 amino acids was chemically synthesized and tested for growth inhibiting, killing and lytic activity in Streptococcus pneumoniae cultures.(152 pages)

L8 ANSWER 8 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-18374 BIOTECHDS
TITLE: New oligonucleotide probes which specifically hybridize to **Staphylococcus aureus histidine kinase** essential genes, useful for developing antibacterial agents, or as probes for detecting the presence a particular gene;
drug screening for use in bacterium infection diagnosis and gene therapy
AUTHOR: BENTON B; MALOUIN F; MARTIN P K; SCHMID M B; SUN D
PATENT ASSIGNEE: ESSENTIAL THERAPEUTICS INC
PATENT INFO: US 6514746 4 Feb 2003
APPLICATION INFO: US 1998-82077 20 May 1998
PRIORITY INFO: US 1998-82077 20 May 1998; US 1995-3798 15 Sep 1995
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-478763 [45]
AB DERWENT ABSTRACT:

NOVELTY - An oligonucleotide probe at least 15 nucleotides in length which specifically hybridizes to a nucleotide which is the same as or complementary to a DNA comprising a sequence of 3731 (I), 702 (II) or 1827 (III) bp given in the specification,especially to (II) and (II).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a **recombinant** bacterial cell containing an artificially inserted DNA construct comprising a nucleotide base sequence which is the same as or complementary to a nucleotide base sequence of the coding region of (I), (II) or (III).

WIDER DISCLOSURE - Also disclosed are the following: (1) screening for an antibacterial agent by determining whether a test compound is active against (I), (II) or (III); (2) diagnosing the presence of a bacterial strain having (I), (II) or (III); (3) treating a bacterial infection in a mammal by administering a compound active against a bacterial gene selected from (I), (II) and (III); and (4) **Staphylococcus aureus** genes termed aspA and espB comprising sequences of 702 and 1827 base pairs respectively.

BIOTECHNOLOGY - Preferred Probe: The coding region comprises (II) or (III).

ACTIVITY - Antibacterial. No supporting data provided.

MECHANISM OF ACTION - Gene therapy.

USE - The probes are useful for the development of antibacterial agents, as probes for identifying the presence of a gene or a bacterium having the particular gene, as reagents to identify DNA chains which contain a sequence corresponding to the probe (e.g. for identifying **clones** having a **recombinant** DNA insert), and as PCR primers.

ADMINISTRATION - Dosage is 0.1-100 mug/ml. Administration can be through oral, rectal, transdermal, vaginal, transmucosal, intestinal, or parenteral (e.g. intramuscular, subcutaneous, intramedullary, intrathecal, intraventricular, intravenous, intraperitoneal, intranasal or intraocular) routes.

EXAMPLE - No relevant example given. (35 pages)

L8 ANSWER 9 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:1087573 SCISEARCH
THE GENUINE ARTICLE: 751GL
TITLE: Chemical communication among bacteria
AUTHOR: Taga M E; Bassler B L (Reprint)
CORPORATE SOURCE: Princeton Univ, Dept Mol Biol, Princeton, NJ 08544 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (25 NOV 2003) Vol. 100, Supp. [2], pp. 14549-14554.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 65

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cell-cell communication in bacteria is accomplished through the exchange of chemical signal molecules called autoinducers. This process, called quorum sensing, allows bacteria to monitor their environment for the presence of other bacteria and to respond to fluctuations in the number and/or species present by altering particular behaviors. Most quorum-sensing systems are species- or group-specific, which presumably prevents confusion in mixed-species environments. However, some quorum-sensing circuits control behaviors that involve interactions among bacterial species. These quorum-sensing circuits can involve both intra- and interspecies communication mechanisms. Finally, anti-quorum-sensing strategies are present in both bacteria and eukaryotes, and these are apparently designed to combat bacteria that rely on cell-cell communication for the successful adaptation to particular niches.

L8 ANSWER 10 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:224073 SCISEARCH
THE GENUINE ARTICLE: 652DR
TITLE: Detection of secreted peptides by using hypothesis-driven multistage mass spectrometry

AUTHOR: Kalkum M; Lyon G J; Chait B T (Reprint)
CORPORATE SOURCE: Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem, 1230 York Ave, New York, NY 10021 USA (Reprint); Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem, New York, NY 10021 USA; Rockefeller Univ, Selma & Lawrence Ruben Lab Synthet Prot Chem, New York, NY 10021 USA
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (4 MAR 2003) Vol. 100, No. 5, pp. 2795-2800.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 53

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A method is presented for the rapid detection and characterization of trace amounts of peptides secreted from microorganisms, including pheromones, virulence factors, and quorum-sensing peptides. The procedure, based on targeted multistage MS, uses a novel matrix-assisted laser desorption/ionization-ion trap mass spectrometer to overcome limitations of current MS methods (limited dynamic range, signal suppression effects, and chemical noise) that impair observation of low abundance peptides from complex biological matrixes. Here, secreted peptides that are hypothesized to be present in the supernatant, but that may not be sufficiently abundant to be observed in single-stage mass spectra, are subjected to multistage MS. Highly specific fragmentation signatures enable unambiguous identification of the peptides of interest and differentiation of the signals from the background. As examples, we demonstrate the rapid (<1 min) determination of the mating type of cells in colonies of Saccharomyces cerevisiae and the elucidation of autoinducing peptides (AIPs) from supernatants of pathogenic Staphylococci. We confirm the primary structures of the agrD encoded cyclic AIPs of **Staphylococcus aureus** for groups 1, 11, and IV and provide direct evidence that the native group-III AIP is a heptapeptide (INCDFLL). We also show that the homologous peptide from Staphylococcus intermedius is a nonapeptide (RIPTSTGFF) with a lactone ring formed through condensation of the serine side chain with the C terminus of the peptide. This is the first demonstration of cyclization in a staphylococcal AIP that occurs via lactone formation. These examples demonstrate the analytical power of the present procedure for characterizing secreted peptides and its potential utility for identifying microorganisms.

L8 ANSWER 11 OF 58 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003570426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14651645
TITLE: Constitutive **expression** of PcsB suppresses the requirement for the essential VicR (YycF) response regulator in Streptococcus pneumoniae R6.
AUTHOR: Ng Wai-Leung; Robertson Gregory T; Kazmierczak Krystyna M; Zhao Jingyong; Gilmour Raymond; Winkler Malcolm E
CORPORATE SOURCE: Department of Biology, Indiana University, Jordan Hall 142, Bloomington, IN 47405, USA.
SOURCE: Molecular microbiology, (2003 Dec) 50 (5) 1647-63.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040302

Entered Medline: 20040301

AB We report several new findings about the function of the essential VicRK two-component regulatory system (TCS) in the human pathogen Streptococcus pneumoniae. The vicR-encoded response regulator, vicK-encoded **histidine kinase** and the protein encoded by the downstream vicX gene are the homologues of the YycF, YycG and YycJ proteins, respectively, studied previously in Bacillus subtilis and **Staphylococcus aureus**. Using a regulatable promoter, we demonstrated that the VicK **histidine kinase** is conditionally required for growth of S. pneumoniae. Likewise, we found that the VicX protein is also conditionally required for growth and probably plays a role in the essential signal transduction pathway mediated by VicR and VicK. Recovery of limited substitutions in the conserved aspartate 52 residue (D52) of VicR was consistent with a requirement for phosphorylation of VicR for growth under some conditions. We applied microarrays to characterize the changes in transcription patterns in bacteria depleted for vicRKX operon **expression**. Our results suggest that the pcsB gene is a target of the VicRK TCS. We present evidence that downregulation of pcsB could account for many of the defects in cell growth, shape, size and morphology observed in bacteria depleted for vicRKX **expression**. Furthermore, constitutive **expression** of pcsB+ suppressed the essential requirement for the VicRK TCS and allowed the isolation of vicR null mutants.

L8 ANSWER 12 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:776164 HCAPLUS
DOCUMENT NUMBER: 139:359758
TITLE: Genes controlled by the essential YycG/YycF two-component system of Bacillus subtilis revealed through a novel hybrid regulator approach
AUTHOR(S): Howell, Alistair; Dubrac, Sarah; Andersen, Kasper Krogh; Noone, David; Fert, Juliette; Msadek, Tarek; Devine, Kevin
CORPORATE SOURCE: Department of Genetics, Smurfit Institute, Trinity College Dublin, Dublin, 2, Ire.
SOURCE: Molecular Microbiology (2003), 49(6), 1639-1655
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The YycG/YycF two-component system, originally identified in Bacillus subtilis, is very highly conserved and appears to be specific to low G + C Gram-pos. bacteria. This system is required for cell viability, although the basis for this and the nature of the YycF regulon remained elusive. Using a combined hybrid regulator/transcriptome approach involving the inducible **expression** of a PhoP'-'YycF chimerical protein in B. subtilis, the authors have shown that **expression** of yocH, which encodes a potential autolysin, is specifically activated by YycF. Gel mobility shift and DNase I footprinting assays were used to show direct binding in vitro of purified YycF to the regulatory regions of yocH as well as ftsAZ, previously reported to be controlled by YycF. Nucleotide sequence anal. and site-directed mutagenesis allowed the authors' to define a potential consensus recognition sequence for the YycF response regulator, composed of two direct repeats: 5'-TGT A/T A A/T/C-N5-TGT A/T A A/T/C-3'. A DNA-motif anal. indicates that there are potentially up to 10 genes within the B. subtilis YycG/YycF regulon, mainly involved in cell wall metabolism and membrane protein synthesis. Among these, YycF was shown to bind directly to the region upstream from the ykvT gene, encoding a potential cell wall hydrolase, and the intergenic region of the tagAB/tagDEF divergon, encoding essential components of teichoic acid biosynthesis. Definition of a potential YycF recognition sequence allowed the authors' to identify likely members of the YycF regulon in other low G + C Gram-pos. bacteria, including several pathogens such as Listeria monocytogenes, **Staphylococcus aureus** and Streptococcus

pneumoniae.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:513309 SCISEARCH
THE GENUINE ARTICLE: 687GZ
TITLE: Autoinduction and signal transduction in the regulation of staphylococcal virulence
AUTHOR: Novick R P (Reprint)
CORPORATE SOURCE: NYU, Sch Med, Dept Microbiol, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA (Reprint); NYU, Sch Med, Dept Med, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR MICROBIOLOGY, (JUN 2003) Vol. 48, No. 6, pp. 1429-1449.
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
ISSN: 0950-382X.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 126
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The accessory genes of **Staphylococcus aureus**, in-cluding those involved in pathogenesis, are controlled by a complex regulatory network that includes at least four two-component systems, one of which, agr , is a quorum sensor, an alternative sigma factor and a large set of transcription factors, including at least two of the superantigen genes, tst and seb. These regulatory genes are hypothesized to act in a time- and population density-dependent manner to integrate signals received from the external environment with the internal metabolic machinery of the cell, in order to achieve the production of particular subsets of accessory/virulence factors at the time and in quantities that are appropriate to the needs of the organism at any given location. From the standpoint of pathogenesis, the regulatory agenda is presumably tuned to particular sites in the host organism. To address this hypothesis, it will be necessary to understand in considerable detail the regulatory interactions among the organism's numerous controlling systems. This review is an attempt to integrate a large body of data into the beginnings of a model that will hopefully help to guide research towards a full-scale test.

L8 ANSWER 14 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-03939 BIOTECHDS
TITLE: Isolation and characterization of inhibitors of the essential **histidine kinase**, YycG in Bacillus subtilis and **Staphylococcus aureus**; vector-mediated gene transfer and **expression** in host cell for antibiotic screening and antibiotic-resistant bacterium infection therapy
AUTHOR: WATANABE T; HASHIMOTO Y; YAMAMOTO K; HIRAO K; ISHIHAMA A; HINO M; UTSUMI R
CORPORATE SOURCE: Kinki Univ; Nippon Inst Biol Sci; Fujisawa Pharmaceut Co Ltd
LOCATION: Utsumi R, Kinki Univ, Grad Sch Agr, Dept Biosci and Biotechnol, 3327-204 Nakamachi, Nara 6318505, Japan
SOURCE: JOURNAL OF ANTIBIOTICS; (2003) 56, 12, 1045-1052
ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AUTHOR ABSTRACT - The set of sensor kinase YycG and response regulator YycF is the only essential two-component system (TCS) in Bacillus subtilis and **Staphylococcus aureus**. We have developed

a screening method for antibacterial agents that inhibit YycG, the essential **histidine kinase** (HK). To increase screening sensitivity, a temperature-sensitive yycF mutant (CNM2000) of B. subtilis with super-sensitivity to HK inhibitors was constructed, which was used for the screening of acetone extracts from 4000 microbes. A total of I I samples showed higher sensitivity to CNM2000 than to wild-type parent 168, and seven of those were characterized to be potent inhibitors against autophosphorylation of YycG. One sample compound was purified and identified as aranorosinol B, a known antibacterial agent against Gram-positive bacteria including B. subtilis and S. aureus. Aranorosinol B inhibited YycG from both B. subtilis and S. aureus with a half-maximum inhibitory concentration (IC50) of 223 and 211 mum, respectively. (8 pages)

L8 ANSWER 15 OF 58 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003448363 EMBASE
TITLE: Turning virulence on and off in Staphylococci.
AUTHOR: Muir T.W.
CORPORATE SOURCE: Dr. T.W. Muir, Lab. of Synthetic Protein Chemistry, The Rockefeller University, 1230 York Avenue, New York, NY 10021, United States. muirt@rockefeller.edu
SOURCE: Journal of Peptide Science, (2003) 9/10 (612-619).
Refs: 21
ISSN: 1075-2617 CODEN: JPSIEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The progress made in a multidisciplinary research programme designed to elucidate the molecular basis of the interaction of **Staphylococcus aureus** secreted autoinducing peptides (AIPs) with their respective cell surface receptors is reviewed. Copyright .COPYRGT. 2003 European Peptide Society and John Wiley & Sons, Ltd.

L8 ANSWER 16 OF 58 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2003373501 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12867749
TITLE: Biochemical characterization of the first essential two-component signal transduction system from **Staphylococcus aureus** and Streptococcus pneumoniae.
AUTHOR: Clausen Valerie A; Bae Weonhye; Throup John; Burnham Martin K R; Rosenberg Martin; Wallis Nicola G
CORPORATE SOURCE: Antimicrobials and Host Defense, GlaxoSmithKline Pharmaceuticals, Collegeville, PA, USA.
SOURCE: Journal of molecular microbiology and biotechnology, (2003) 5 (4) 252-60.
Journal code: 100892561. ISSN: 1464-1801.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030812
Last Updated on STN: 20030905
Entered Medline: 20030904

AB The YYCFG two-component signal transduction system (TCSTS) has been shown to be essential to the viability of several gram-positive bacteria. However, the function of the gene pair remains unknown. Interestingly, while both components are essential to **Staphylococcus aureus** and Bacillus subtilis, only the response regulator (YYCF)

is essential to Streptococcus pneumoniae. To study this essential TCSTS further, the S. pneumoniae and S. aureus truncated YycG **histidine kinase** and full-length YycF response regulator proteins were characterized at a biochemical level. The **recombinant** proteins from both organisms were **expressed** in Escherichia coli and purified. The YycG autophosphorylation activities were activated by ammonium. The apparent K(m)(ATP) of S. aureus YycG autophosphorylation was 130 microM and S. pneumoniae was 3.0 microM. Each had similar K(cat)values of 0.036 and 0.024 min(-1), respectively. Cognate phosphotransfer was also investigated indicating different levels of the phosphorylated YycG intermediates during the reaction. The S. pneumoniae YycG phosphorylated intermediate was not detectable in the presence of its cognate YycF, while phosphorylated S. aureus YycG and YycF were detected concurrently. In addition, noncognate phosphotransfer was demonstrated between the two species. These studies thoroughly compare the essential YycFG TCSTS from the two species at the biochemical level and also establish methods for assaying the activities of these antibacterial targets.

L8 ANSWER 17 OF 58 BIOSIS

ACCESSION NUMBER: 2003:517200 BIOSIS
DOCUMENT NUMBER: PREV200300519820
TITLE: Subcellular localization of SrrAB, a novel two-component regulatory system in **Staphylococcus aureus**.
AUTHOR(S): Pragman, A. A. [Reprint Author]; Schlievert, P. M. [Reprint Author]
CORPORATE SOURCE: University of Minnesota, Minneapolis, MN, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-066. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

AB Background: SrrAB is a novel two-component system that regulates S. aureus virulence factors in response to oxygen. SrrA, the putative response regulator, is predicted to encode a DNA-binding protein. SrrB, the putative **histidine kinase**, is predicted to encode a membrane-spanning protein. We hypothesize that SrrA is localized in the S. aureus cytoplasm while SrrB is localized to the membrane. Methods: Polyclonal antibodies were raised against **recombinant** SrrA as well as the predicted extracellular domain of SrrB by immunizing Dutch Belted Rabbits. S. aureus strains DU5875 and DU5875 (pJMY11) were grown microaerobically to post-exponential phase in order to induce maximal **expression** of SrrAB. Cells were lysed by sonication, and membrane and cytoplasmic extracts of both strains were electrophoresed and blotted by Western analysis with SrrA and SrrB antibodies. S. aureus MN8 was immunostained with SrrB or a pre-immune control antibody and visualized by chromogenic peroxidase staining. Results: Both strains DU5875 and DU5875 (pJMY11) demonstrated that SrrA as well as SrrB are localized to the membrane fraction when bacteria are lysed by sonication. SrrA is likely also present in the cytoplasm. Ongoing work will address the localization of SrrAB when other methods are used to lyse the bacteria. S. aureus MN8 demonstrated strong chromogenic staining following incubation with SrrB, compared with control antibody. Scanning electron microscopy studies using the SrrB antibody to visualize the membrane distribution of SrrB are

in progress. Conclusion: S. aureus SrrB is localized to the bacterial cell membrane. The predicted extracellular domain of SrrB is found on the external cell surface. Sonicated cell extracts indicate that SrrA is also localized to the cell membrane.

L8 ANSWER 18 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:517239 BIOSIS
DOCUMENT NUMBER: PREV200300519832
TITLE: Two-component gene regulation in the biology of Enterococcus faecalis.
AUTHOR(S): Hancock, L. E. [Reprint Author]; Perego, M. [Reprint Author]
CORPORATE SOURCE: Scripps Research Institute, La Jolla, CA, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-078. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

AB Enterococci are commensals within the mammalian intestinal tract, but also possess the ability to cause disease in compromised hosts, emerging in recent years as a leading nosocomial pathogen. In association with this emergence has been the acquisition of resistance determinants to multiple antibiotics, making infections caused by these organisms clinically challenging. The ability of these organisms to adapt and respond to different environmental stimuli, including the host environment led us to investigate the role of two-component signal transduction in the regulation of gene **expression** in Enterococcus faecalis. Using a bioinformatic approach we identified 17 two-component systems (TCS), consisting of a sensory **histidine kinase** and the cognate response regulator, as well as an additional orphan response regulator. In an effort to identify the potential function of each TCS in the biology of E. faecalis strain V583, we constructed insertionally inactivated mutations in each of the response regulators. We were unable to inactivate one response regulator. This response regulator shares extensive sequence similarity with the Bacillus subtilis, Staphylcoccus aureus, Streptococcus pneumoniae YycF protein, previously shown to be essential for viability in these Gram-positive microorganisms. The biological effect of the remaining mutations was assessed using a number of assays, including antibiotic resistance, biofilm formation, as well as growth under acidic and high salt environments. We identified several TCS related to antibiotic resistance, and found one TCS which controls the initiation of biofilm development by E. faecalis.

L8 ANSWER 19 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2002-10378 BIOTECHDS
TITLE: Assay for detecting compounds that modulates **histidine kinase** activity, by contacting compound with kinase and substrate, and monitoring the rate or absolute amount of phosphate transfer by kinase to the substrate;
plasmid pMal-(RTM)-c2-mediated gene transfer and **expression** in Escherichia coli for drug screening
AUTHOR: GOLDSCHMIDT R; LOELOFF M
PATENT ASSIGNEE: GOLDSCHMIDT R; LOELOFF M
PATENT INFO: US 2002004214 10 Jan 2002
APPLICATION INFO: US 1999-733731 21 Dec 1999

PRIORITY INFO: US 2000-733731 8 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-171025 [22]

AB DERWENT ABSTRACT:

NOVELTY - Assay for detecting compounds that modulate **histidine kinase** (HK) enzymatic activity or interaction of HK with its cognate response regulator protein, involves contacting a compound (C) with HK and HK substrate, isolating HK substrate by affinity capture and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer by HK to the substrate in the presence of (C).

DETAILED DESCRIPTION - Assay for detecting compounds that modulate **histidine kinase** (HK) enzymatic activity or interaction of HK with its cognate response regulator protein, involves: (a) identifying compounds that modulate EspB **histidine kinase** enzymatic activity, by admixing a test compound, an EspB **histidine kinase** fusion protein comprising an EspB **histidine kinase** catalytic domain and an affinity capture domain, and a high energy phosphate source, incubating the compound with **histidine kinase** fusion protein and high energy phosphate source, isolating the EspB **histidine kinase** fusion protein by affinity isolation, and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer to the EspB **histidine kinase** by autophosphorylation in the presence of the compound; or (b) identifying compounds that modulate **histidine kinase** enzymatic activity or modulate interaction of the kinase with its cognate response regulator protein, by admixing a test compound, an EspA cognate **histidine kinase** or its functional derivative, where the kinase has functional **histidine kinase** activity, an EspA fusion protein comprising an EspA phosphorylation domain and an affinity capture domain, and a high energy phosphate source, incubating the compound with **histidine kinase** or its derivative, the EspA fusion protein and the high energy phosphate source, isolating the EspA fusion protein by affinity isolation, and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer by the kinase to the EspA fusion protein in the presence of the compound. An INDEPENDENT CLAIM is also included for a **histidine kinase** fusion protein (I) comprising a protein domain of the espB gene or its functional derivative having functional catalytic activity and a protein or peptide having at least one affinity capture domain.

WIDER DISCLOSURE - The following are also disclosed as new: (1) construction of **histidine kinase** fusion proteins that maintain catalytic activity, create at least one affinity capture domain and eliminate a hydrophobic membrane-spanning domain contained with the native protein; (2) a cognate response regulator fusion proteins comprising a protein domain of a cognate response regulator that maintains functional transphosphorylation activity, fused to a protein or peptide molecule having affinity capture domain; and (3) **histidine kinase** fusion protein comprising a protein domain or its functional derivative having functional catalytic activity and a protein or peptide having at least one affinity capture domain.

BIOTECHNOLOGY - Preferred Method: The method is conducted in a single scintillant - impregnated or coated vessel. The phosphorylated EspB **histidine kinase** or the EspA fusion protein is isolated by affinity capture onto the surface of the vessel. Preferred Protein: The affinity capture protein or peptide is selected from malE gene of Escherichia coli, the glutathione S-transferase encoding gene of Schistosoma japonicum, and hexahistidine. The EspB **histidine kinase** catalytic domain comprises the carboxy terminal 311 amino acids of the espB gene. The EspA cognate **histidine kinase** is EspB, its ortholog or a paralog that can transphosphorylate EspA. The protein domain of (I) comprises about the

carboxy terminal 397 or 311 amino acids of the espB gene.

ACTIVITY - Antibacterial. No suitable data is given in the source material.

MECHANISM OF ACTION - Modulator of **histidine kinase** activity (claimed).

USE - The method is useful for detecting modulators of **histidine kinase** enzyme activity or its interaction with its cognate response regulator protein (claimed). The identified compounds are useful to inhibit growth and kill bacteria that cause infectious disease, while minimizing any potential toxicity.

ADVANTAGE - The method is a robust, sensitive assay of simple design that is easily automated and an assay that can be easily modified to allow different **histidine kinase** and response regulator targets to be tested without significant modification to the design.

EXAMPLE - To construct affinity capture protein-**histidine kinase** (MalE-EspB) fusions, pMal-(RTM)-c2 plasmid was used. Two amplifications of espB gene were generated through polymerase chain reaction (PCR) amplification of DNA from **Staphylococcus aureus** strain COL using plaque forming units (Pfu) DNA polymerase and pairs of primers given in the specification. The first amplicon, obtained using primers HKFM02 and HKBM02, encoded the 397 C-terminal amino acids of EspB, starting at Asp212. The two primers had BamHI and HindIII sites, respectively, to allow the **cloning** into the same sites of the vector maintaining the proper reading frame for the protein fusion. The second amplicon, obtained using primers HKFM03 and HKBM02 encoded the 311 C-terminal amino acids of EspB, starting at Met298. Similar to the first case, the two primers had BamHI and HindIII sites, respectively, to allow the **cloning** into the same sites of the vector maintaining the proper reading frame for the protein fusion. The malE-espB fusion gene was transformed into DH5alpha cells for fusion protein **expression**. One inoculation loop with transformed cells was inoculated into 125 ml of LB medium in the presence of 100 microg/ml of ampicillin. The culture was incubated at 37 degrees C with shaking overnight. The cells were induced for MalE-EspB **expression** by adding IPTG (isopropyl beta-d-thiogalactopyranoside) to a final concentration of 0.5 mM and incubated with shaking at 37 degrees C. The cells were then harvested after 4 hours of culture. The media was centrifuged and then the pellet was isolated and stored at -80 degrees C for later purification. (17 pages)

L8 ANSWER 20 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:359080 SCISEARCH
THE GENUINE ARTICLE: 543NH
TITLE: rgf encodes a novel two-component signal transduction system of Streptococcus agalactiae
AUTHOR: Spellerberg B (Reprint); Rozdzinski E; Martin S; Weber-Heynemann J; Lutticken R
CORPORATE SOURCE: Univ Ulm, Dept Med Microbiol & Hyg, Robert Koch Str 8, D-89081 Ulm, Germany (Reprint); Univ Ulm, Dept Med Microbiol & Hyg, D-89081 Ulm, Germany; Univ Hosp Aachen, Inst Med Microbiol, D-52057 Aachen, Germany; Univ Hosp Aachen, Natl Reference Ctr Streptococci, D-52057 Aachen, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: INFECTION AND IMMUNITY, (MAY 2002) Vol. 70, No. 5, pp. 2434-2440.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 32

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The adhesion of gram-positive bacteria to extracellular matrix (ECM) proteins is regarded as an important determinant of pathogenicity. A comparison of the adhesion of Streptococcus agalactiae strain O90R to different ECM proteins showed that the most pronounced binding could be observed for immobilized fibrinogen. To investigate the genetic determinants of S. agalactiae fibrinogen binding, a pGhost9:ISS1 mutant library was screened for mutants displaying reduced agglutination of fibrinogen-coated latex beads. A putative two-component signal transduction system was identified and designated rgfBDAC. It comprises genes encoding a putative response regulator of 218 amino acids and a putative **histidine kinase** of 426 amino acids.
Comparison of the deduced proteins with the GenBank database revealed a significant similarity to quorum-sensing systems of gram-positive pathogens. Transcription analysis of the rgf locus showed that the encoding genes are located on one transcript. To further characterize the influence of the putative **histidine kinase** encoded in the rgf locus on the adhesion of S. agalactiae to immobilized fibrinogen, a targeted mutant of rgfC was generated. In comparison to the wild-type strain this mutant demonstrated altered fibrinogen binding capacities depending on bacterial cell density. Transcription analysis of secreted and surface-localized S. agalactiae proteins in the wild type and the rgfC mutant strain revealed that mRNA levels of the C5a peptidase gene sepB were increased in the mutant strain while the transcription of the secreted CAMP factor gene cfb was unaffected by this mutation. Based on these results, we hypothesize that rgf regulates the **expression** of bacterial cell surface components.

L8 ANSWER 21 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:652704 SCISEARCH
THE GENUINE ARTICLE: 579BC
TITLE: Recent progress in Bacillus subtilis two-component regulation
AUTHOR: Ogura M; Tanaka T (Reprint)
CORPORATE SOURCE: Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci, Orido 3-20-1, Shizuoka 4248610, Japan (Reprint); Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci, Shizuoka 4248610, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: FRONTIERS IN BIOSCIENCE, (AUG 2002) Vol. 7, pp. D1815-D1824.
Publisher: FRONTIERS IN BIOSCIENCE INC, C/O NORTH SHORE UNIV HOSPITAL, BIOMEDICAL RESEARCH CENTER, 350 COMMUNITY DR, MANHASSET, NY 11030 USA.
ISSN: 1093-9946.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 77

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two-component regulatory systems serve to control gene **expression** in response to environmental and physiological changes. They are widespread among a variety of organisms and most often found in prokaryotes. One of the gram-positive microorganisms Bacillus subtilis is a well-studied bacterium whose complete nucleotide sequence has been determined. Thus, it is now possible to study transcription of the whole genome with microarray analysis. In this review we summarize the recent progress in B. subtilis two-component regulatory systems by describing the known systems and those for which the function was recently assigned. Also included is an attempt to construct a partial transcriptional network involving several two-component systems. The studies described here are based on the data from traditional genetics and biochemistry, and from microarray analysis of 29 two-component systems.

L8 ANSWER 22 OF 58 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002080831 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11807070
TITLE: Repression of the **Staphylococcus aureus** accessory gene regulator in serum and in vivo.
AUTHOR: Yarwood Jeremy M; McCormick John K; Paustian Michael L; Kapur Vivek; Schlievert Patrick M
CORPORATE SOURCE: Department of Microbiology, Medical School, University of Minnesota, Minneapolis, Minnesota, USA.
CONTRACT NUMBER: HL36611 (NHLBI)
SOURCE: Journal of bacteriology, (2002 Feb) 184 (4) 1095-101. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020128
Last Updated on STN: 20020320
Entered Medline: 20020319

AB Subgenomic DNA microarrays were employed to evaluate the **expression** of the accessory gene regulator (agr locus) as well as multiple virulence-associated genes in **Staphylococcus aureus**. Gene **expression** was examined during growth of S. aureus in vitro in standard laboratory medium and rabbit serum and in vivo in subcutaneous chambers implanted in either nonimmune rabbits or rabbits immunized with staphylococcal enterotoxin B. **Expression** of RNAIII, the effector molecule of the agr locus, was dramatically repressed in serum and in vivo, despite the increased **expression** of secreted virulence factors sufficient to cause toxic shock syndrome (TSS) in the animals. Statistical analysis and clustering of virulence genes based on their **expression** profiles in the various experimental conditions demonstrated no positive correlation between the **expression** of agr and any staphylococcal virulence factors examined. Disruption of the agr locus had only a minimal effect on the **expression** in vivo of the virulence factors examined. An effect of immunization on the **expression** of agr and virulence factors was also observed. These results suggest that agr activation is not necessary for development of staphylococcal TSS and that regulatory circuits responding to the in vivo environment override agr activity.

L8 ANSWER 23 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 6
ACCESSION NUMBER: 2002:267761 BIOSIS
DOCUMENT NUMBER: PREV200200267761
TITLE: **Histidine kinases** as targets for new antimicrobial agents.
AUTHOR(S): Matsushita, Masayuki [Reprint author]; Janda, Kim D. [Reprint author]
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute and Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, BCC-582, La Jolla, CA, 92037, USA kdjanda@scripps.edu
SOURCE: Bioorganic and Medicinal Chemistry, (April, 2002) Vol. 10, No. 4, pp. 855-867. print. ISSN: 0968-0896.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002

AB The emergence and spread of hospital acquired multi drug resistant bacteria present a need for new antibiotics with innovative mode of action. Advances in molecular microbiology and genomics have led to the

identification of numerous bacterial genes coding for proteins that could potentially serve as targets for antibacterial compounds. **Histidine kinase** promoted two-component systems are extremely common in bacteria and play an important role in essential signal transduction for adapting to bacterial stress. Since signal transduction in mammals occurs by a different mechanism, inhibition of **histidine kinases** could be a potential target for antimicrobial agents. This review will summarize our current knowledge of the structure and function of **histidine kinase** and the development of antibiotics with a new mode of action: targeting **histidine kinase** promoted signal transduction and its subsequent regulation of gene **expression** system.

L8 ANSWER 24 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:756564 SCISEARCH
THE GENUINE ARTICLE: 591TY
TITLE: Two-component and phosphorelay signal-transduction systems as therapeutic targets
AUTHOR: Stephenson K (Reprint); Hoch J A
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt Med, La Jolla, CA 92037 USA
COUNTRY OF AUTHOR: USA
SOURCE: CURRENT OPINION IN PHARMACOLOGY, (OCT 2002) Vol. 2, No. 5, pp. 507-512.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
ISSN: 1471-4892.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 63
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two-component and phosphorelay signal-transduction systems of pathogenic bacteria control the **expression** of genes encoding virulence factors and essential functions. Recent systematic gene inactivation studies have confirmed the integral role of two-component systems in the pathogenesis of diseases caused by several microorganisms and highlighted the validity of using these systems as targets for therapeutic intervention. Structural studies of signal-transduction proteins have recently revealed common features that may allow rational drug design for therapeutic intervention. In particular, the conserved domains of response regulators may represent the best targets for inhibition.

L8 ANSWER 25 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:858990 HCAPLUS
DOCUMENT NUMBER: 138:148485
TITLE: Regulatory relationship of two-component and ABC transport systems and clustering of their genes in the Bacillus/Clostridium group, suggest a functional link between them
AUTHOR(S): Joseph, Pascale; Fichant, Gwennaele; Quentin, Yves; Denizot, Francois
CORPORATE SOURCE: Laboratoire de Chimie Bacterienne, Institut de Biologie Structurale et Microbiologie, CNRS 31, Marseille, 13402, Fr.
SOURCE: Journal of Molecular Microbiology and Biotechnology (2002), 4(5), 503-513
CODEN: JMMBFF; ISSN: 1464-1801
PUBLISHER: Horizon Scientific Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB On the Bacillus subtilis chromosome there are five examples of genes encoding two-component systems with response regulators of the OmpR family adjacent to genes encoding sub-family 9 ABC transport systems. Three of these (yts, yvc, yxd) are very similar in gene organization and in sequence. The authors demonstrate that the TCS and ABC transporter genes do not belong to the same transcriptional unit. The ABC transport and TCS systems are functionally linked, each response regulator controlling the **expression** of its cognate ABC transporter genes but not its own. Anal. of 48 bacterial genomes revealed that such family clusters only exist in the Bacillus/Clostridium group. Evolutionary analyses indicated that almost all clustered OmpR response regulators constitute two groups ("GI" and "GII") whereas almost all clustered sub-family 9 nucleotide-binding domains belong to two other groups ("9A" and "9B"). Interestingly, there is a mutually exclusive clustering between genes encoding "GI" or a "GII" response regulators and genes encoding "9A" or a "9B" nucleotide binding proteins. The authors propose that a two-component system and its cognate ABC transporter genes have evolved as a unit in Bacillus/Clostridium, both systems participating in a common physiol. process.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:602183 SCISEARCH
THE GENUINE ARTICLE: 571KL
TITLE: Virulence- and antibiotic resistance-associated two-component signal transduction systems of Gram-positive pathogenic bacteria as targets for antimicrobial therapy
AUTHOR: Stephenson K; Hoch J A (Reprint)
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, Div Cellular Biol, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt Med, Div Cellular Biol, La Jolla, CA 92037 USA
COUNTRY OF AUTHOR: USA
SOURCE: PHARMACOLOGY & THERAPEUTICS, (FEB-MAR 2002) Vol. 93, No. 2-3, pp. 293-305.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0163-7258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 92

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two-component signal transduction systems are central elements of the virulence and antibiotic resistance responses of opportunistic bacterial pathogens. These systems allow the bacterium to sense and respond to signals emanating from the host environment and to modulate the repertoire of genes **expressed** to allow invasion and growth in the host. The integral role of two-component systems in virulence and antibiotic sensitivity, and the existence of essential two-component systems in several pathogenic bacteria, suggests that these systems may be novel targets for antimicrobial intervention. This review discusses the potential use of two-component systems as targets for antimicrobial therapy against Gram-positive pathogens and the current status in the development of inhibitors specific for these systems.

L8 ANSWER 27 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:613874 HCAPLUS
TITLE: Turning virulence on and off in Staphylococci
AUTHOR(S): Muir, Tom W.
CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, Rockefeller University, New York City, NY, 10021, USA

SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), BIOL-102. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB The emergence of methicillin-resistant and, more recently, vancomycin-resistant strains of **Staphylococcus aureus** represents an enormous threat to public health. Consequently, there is a pressing need to identify new types of antibacterial agents and it has been suggested that interference with the **expression** of virulence may represent a promising antibacterial modality. Staphylococcal virulence is regulated by a two-component quorum sensing system, agr, activated by a self-coded autoinducing peptide (AIP). The agr system is widely divergent and is unique in that variant AIPs cross-inhibit agr activation in heterologous combinations. Cross-inhibition, but not self-activation, is widely tolerant of structural diversity in the AIPs so that these two processes must involve different mechanisms of interaction with the resp. receptors. We have used a combination of mol. genetics, protein chemical and chemical synthesis to establish that these AIPs from S. aureus contain a thiolactone structure, and that this feature is absolutely necessary for full biol. activity. Moreover, structure-activity studies have allowed key aspects within the AIP and its **histidine-kinase** receptor, AgrC, involved in the differential activation and inhibition functions to be identified. This has led to the rational design of global inhibitors of virulence within the Staphylococci as well as the development of a model for receptor agonism and antagonism.

L8 ANSWER 28 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:452628 BIOSIS
DOCUMENT NUMBER: PREV200100452628
TITLE: **Histidine kinase** of **Staphylococcus aureus**.
AUTHOR(S): Wallis, Nicola Gail [Inventor]; Traini, Christopher Michael [Inventor]; Kosmatka, Anna Lisa [Inventor]; Shilling, Lisa Kathleen [Inventor]; Warren, Richard Lloyd [Inventor]
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation, Philadephia, PA, USA; SmithKline Beecham plc, Brenford, UK
PATENT INFORMATION: US 6270992 August 07, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 7, 2001) Vol. 1249, No. 1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002

AB The invention provides **Histidine kinase** polypeptides and polynucleotides encoding **Histidine kinase** polypeptides and methods for producing such polypeptides by **recombinant** techniques. Also provided are methods for utilizing **Histidine kinase** polypeptides to screen for antibacterial compounds.

L8 ANSWER 29 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:378355 BIOSIS
DOCUMENT NUMBER: PREV200100378355
TITLE: **Histidine kinase**, 636 HK, of **staphylococcus aureus**.
AUTHOR(S): Burnham, Martin K R [Inventor]; Palmer, Leslie Marie [Inventor]; Throup, John Peter [Inventor, Reprint author];

Van Horn, Stephanie [Inventor]; Warren, Richard Lloyd [Inventor]
CORPORATE SOURCE: Royersford, PA, USA
ASSIGNEE: SmithKline Beecham Corporation
PATENT INFORMATION: US 6194174 February 27, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Aug 2001
Last Updated on STN: 19 Feb 2002

AB The invention provides 636 HK polypeptides and polynucleotides encoding 636 HK polypeptides and methods for producing such polypeptides by **recombinant** techniques. Also provided are methods for utilizing 636 HK polypeptides to screen for antibacterial compounds.

L8 ANSWER 30 OF 58 MEDLINE on STN
ACCESSION NUMBER: 2001469003 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11513618
TITLE: The srhSR gene pair from **Staphylococcus aureus**: genomic and proteomic approaches to the identification and characterization of gene function.
AUTHOR: Throup J P; Zappacosta F; Lunsford R D; Annan R S; Carr S A; Lonsdale J T; Bryant A P; McDevitt D; Rosenberg M; Burnham M K
CORPORATE SOURCE: Anti-infectives Research, GlaxoSmithKline Pharmaceuticals Research and Development, Collegeville, Pennsylvania 19426, USA.. John_Throup-1@sbphrd.com
SOURCE: Biochemistry, (2001 Aug 28) 40 (34) 10392-401. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010830
Last Updated on STN: 20030325
Entered Medline: 20010927

AB Systematic analysis of the entire two-component signal transduction system (TCSTS) gene complement of **Staphylococcus aureus** revealed the presence of a putative TCSTS (designated SrhSR) which shares considerable homology with the ResDE His-Asp phospho-relay pair of Bacillus subtilis. Disruption of the srhSR gene pair resulted in a dramatic reduction in growth of the srhSR mutant, when cultured under anaerobic conditions, and a 3-log attenuation in growth when analyzed in the murine pyelonephritis model. To further understand the role of SrhSR, differential display two-dimensional gel electrophoresis was used to analyze the cell-free extracts derived from the srhSR mutant and the corresponding wild type. Proteins shown to be differentially regulated were identified by mass spectrometry in combination with protein database searching. An srhSR deletion led to changes in the **expression** of proteins involved in energy metabolism and other metabolic processes including arginine catabolism, xanthine catabolism, and cell morphology. The impaired growth of the mutant under anaerobic conditions and the dramatic changes in proteins involved in energy metabolism shed light on the mechanisms used by S. aureus to grow anaerobically and indicate that the staphylococcal SrhSR system plays an important role in the regulation of energy transduction in response to changes in oxygen availability. The combination of proteomics, bio-informatics, and microbial genetics employed here represents a powerful set of techniques which can be applied to the study of bacterial gene function.

L8 ANSWER 31 OF 58 MEDLINE on STN

ACCESSION NUMBER: 2001337274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11136460
TITLE: Group A streptococcal growth phase-associated virulence factor regulation by a novel operon (Fas) with homologies to two-component-type regulators requires a small RNA molecule.
AUTHOR: Kreikemeyer B; Boyle M D; Buttaro B A; Heinemann M; Podbielski A
CORPORATE SOURCE: Department of Medical Microbiology and Hygiene, University Hospital Ulm, Robert-Koch-Str. 8, D-89081 Ulm, Germany.
SOURCE: Molecular microbiology, (2001 Jan) 39 (2) 392-406. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB A novel growth phase-associated two-component-type regulator, Fas (fibronectin/fibrinogen binding/haemolytic activity/streptokinase regulator), of Streptococcus pyogenes was identified in the M1 genome sequence, based on homologies to the histidine protein kinase (HPK) and response regulator (RR) part of the **Staphylococcus aureus** Agr and Streptococcus pneumoniae Com quorum-sensing systems. The fas operon, present in all 12 tested M serotypes, was transcribed as polycystronic message (fasBCA) and contained genes encoding two potential HPKs (FasB and FasC) and one RR (FasA). Downstream of fasBCA, we identified a small 300 nucleotide monocistronic transcript, designated fasX, that did not appear to encode true peptide sequences. Measurements of luciferase promoter fusions revealed a growth phase-associated transcription of fasBCA and fasX, with peak activities during the late exponential phase. Insertional mutagenesis disrupting fasBCA and fasA led to a phenotype similar to agr-null mutations in S. aureus, with prolonged **expression** of extracellular matrix protein-binding adhesins and reduced **expression** of secreted virulence factors such as streptokinase and streptolysin S. In addition, fasX transcription was dependent on the RR FasA; however, deletion mutagenesis of fasX resulted in a similar phenotype to that of the fasBCA or fasA mutants. Complementation of the fasX deletion mutant, with the fasX gene **expressed** in trans from a plasmid, restored the wild-type fasBCA regulation pattern. This strongly suggested that fasX, a putative non-translated RNA, is the main effector molecule of the fas regulon. However, using spent culture supernatants from wild-type and fas mutant strains, we were not able to show an influence on the logarithmic growth phase **expression** of fas and dependent genes. Thus, despite structural and functional similarities between fas and agr, to date the fas operon appears not to be involved in group A streptococcal (GAS) quorum-sensing regulation.

L8 ANSWER 32 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:455510 HCAPLUS
DOCUMENT NUMBER: 135:192773
TITLE: Characterization of bacteriocin N15 produced by Enterococcus faecium N15 and **cloning** of the related genes
AUTHOR(S): Losteinkit, Chanvadee; Uchiyama, Keiji; Ochi, Shuichiro; Takaoka, Tomoyo; Nagahisa, Keisuke; Shioya, Suteaki
CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Osaka University, Suita, 565-0871, Japan
SOURCE: Journal of Bioscience and Bioengineering (2001), 91(4), 390-395

CODEN: JBBIF6; ISSN: 1389-1723
PUBLISHER: Society for Bioscience and Bioengineering, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enterococcus faecium N15 was isolated from nuka (Japanese rice-bran paste), which is utilized as starter in the fermenting of vegetables, and was found to produce a bacteriocin that exhibited a broad spectrum of activity, including activity against Listeria monocytogenes and Bacillus circulans JCM2504. The bacteriocin was sensitive to proteases (α-chymotrypsin, proteinase K, trypsin, and pepsin) and α-amylase, but it was resistant to lipase. The bacteriocin was resistant to heat treatment at 100°C for 2 h, but its activity was completely lost after autoclaving at 121°C for 15 min. It was active over a wide pH range from 2.0 to 10.0. The bacteriocin showed bactericidal activity against Lactobacillus sake JCM1157 at a concentration of 40 AU/mL. Its mol. weight was estimated by SDS-PAGE to be about 3-5 kDa. PCR primers were designed based on the conserved amino acid sequences of class IIa bacteriocins. A 3-kb DNA fragment was amplified and three open reading frames (ORFs) were found. The first encodes a probable immunity protein of 103 amino acid residues and shows complete homol. with the putative immunity protein of E. faecium DPC1146. The second and third ORFs resp. encode a probable transposase gene and an inducing factor. The upstream region of the immunity gene, in which the bacteriocin structural gene is located, was amplified. A homol. search revealed that the bacteriocin produced by E. faecium N15 exhibits complete identity to enterocin A, a bacteriocin produced by E. faecium DPC1146. PCR using the primers designed in this study is a rapid and sufficient method of screening for bacteriocin-producing strains.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 7

ACCESSION NUMBER: 2001-03236 BIOTECHDS
TITLE: **Histidine-kinase** polypeptides and polynucleotides, useful for treating bacterial infections caused by **Staphylococcus aureus** such as otitis media, thyroiditis, empyema and for screening antibacterial compounds;
the use of **recombinant histidine-kinase**
AUTHOR: Throup J P; Palmer L M; Burnham M K; Warren R L; van Horn S
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: WO 2000068360 16 Nov 2000
APPLICATION INFO: WO 2000-US12862 11 May 2000
PRIORITY INFO: US 1999-310275 12 May 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-016089 [02]

AB An isolated **histidine-kinase** (636HK) protein (I) is claimed. (I) contains a sequence having at least 95% identity to a fully defined sequence (S1) of 608 amino acids over its entire length, a sequence containing S1, or a sequence encoded by a **recombinant** polynucleotide with a fully defined sequence of 1,827 bp. Also claimed are: an isolated polynucleotide (II); diagnosing or prognosing a disease or a susceptibility to a disease in an individual related to **expression** or activity of (I); production of (I); producing a host cell by an **expression** system or its membrane **expressing** (I); a host cell or a membrane **expressing** (I); an antibody immunospecific for (I); screening to identify compounds that agonize or inhibit the function (I); and an agonist or antagonist to (I). (I) is useful to treat an individual in need of enhanced activity

or **expression** of or immunological response to (I). The antagonists or agonists of (I) are useful for treating microbial infections. (I) and (II) are useful as research reagent material for discovery of treatment and diagnosis. (I), (II) and agonists and antagonists are useful in treatment of Helicobacter pylori infection, etc. (40pp)

L8 ANSWER 34 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 8
ACCESSION NUMBER: 2001-00945 BIOTECHDS
TITLE: **Histidine-kinase** family polypeptides obtained from **Staphylococcus aureus**, useful for developing antibacterial compounds; vector-mediated gene transfer and **expression** in host cell, antibody, agonist and antagonist, appl. cancer and bacterium infection therapy
AUTHOR: Wallis N G
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA.
PATENT INFO: WO 2000056865 28 Sep 2000
APPLICATION INFO: WO 2000-US6206 9 Mar 2000
PRIORITY INFO: US 1999-274058 22 Mar 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-638259 [61]
AB A **histidine-kinase** family protein containing a sequence that is or has at least 95% identity to a sequence of 346 amino acids, or a protein encoded by nucleotides 222-1,258 of a 1,500 bp sequence, is new. Also claimed are: a polynucleotide encoding the protein **expressed** by **histidine-kinase** gene contained in **Staphylococcus aureus**; diagnosing or prognosing a disease or susceptibility to a disease in an individual related to **expression** or activity of the protein; production of the protein; producing a host cell containing an **expression** system, or membrane, by transforming or transfecting a cell with an **expression** system containing the polynucleotide; a host cell; an antibody; screening to identify compounds that agonize or antagonize protein function; and an agonist or antagonist. The protein, polynucleotide and agonists or antagonists are useful for treating an individual in need of enhanced activity, **expression** or immunological response to the protein. The protein and its agonist or antagonist are useful for treating bacterial infections, which in turn is useful in treating bacterial induced cancers, ulcers and gastritis. (39pp)

L8 ANSWER 35 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 9
ACCESSION NUMBER: 2001-00532 BIOTECHDS
TITLE: New **histidine-kinase** polypeptide and polynucleotide, useful for treating, preventing or diagnosing microbial diseases, especially infections caused by **Staphylococcus aureus**, e.g. otitis media, thyroiditis or wound infection; vector-mediated gene transfer and **expression** in host cell, antibody, agonist and antagonist
AUTHOR: Wallis N G
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philladelphia, PA, USA.
PATENT INFO: WO 2000056154 28 Sep 2000
APPLICATION INFO: WO 2000-US6133 8 Mar 2000
PRIORITY INFO: US 1999-272414 19 Mar 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-611569 [58]

AB A **Staphylococcus aureus** WCUH-29 (NCIMB 40771) **histidine-kinase** (hk-I) protein containing a 583 amino acid sequence, a sequence with at least 95% identity or a sequence encoded by a **recombinant** polynucleotide containing nucleotides 87-1,835 bp of a 2,244 bp sequence, is new. Also claimed are: treating an individual in need of enhanced or inhibited activity or **expression** of hk-I; diagnosing or prognosing a disease or susceptibility to a disease related to **expression** or activity of hk-I in an individual; producing hk-I; producing a host cell containing an **expression** system or membrane **expressing** hk-I; a host cell or a membrane **expressing** hk-I; an antibody; screening or identifying compounds that agonize or inhibit the function of hk-I; and an agonist or antagonist of hk-I. The protein and polynucleotide are useful for treating, preventing or diagnosing microbial diseases, especially infections caused by **Staphylococcus aureus**. These diseases include otitis, media, thyroiditis, cerebral abscess, toxic shock syndrome, etc. (39pp)

L8 ANSWER 36 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:239703 BIOSIS
DOCUMENT NUMBER: PREV200100239703
TITLE: Sensor **histidine kinase** of **Staphylococcus Aureus.**
AUTHOR(S): Wallis, Nicola Gail [Inventor]
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation
PATENT INFORMATION: US 6127147 October 03, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 3, 2000) Vol. 1239, No. 1. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2001
Last Updated on STN: 18 Feb 2002

AB The invention provides **histidine kinase** polypeptides and DNA (RNA) encoding **histidine kinase** polypetides and methods for producing such polypeptides by **recombinant** techniques. Also provided are methods for utilizing **histidine kinase** polypeptides to screen for antibacterial compounds.

L8 ANSWER 37 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:70585 BIOSIS
DOCUMENT NUMBER: PREV200100070585
TITLE: Sensor **histidine kinase** of **Staphylococcus aureus.**
AUTHOR(S): Wallis, Nicola Gail [Inventor]
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation; SmithKline Beecham, p.l.c., UK
PATENT INFORMATION: US 6071894 June 06, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 6, 2000) Vol. 1235, No. 1. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Feb 2001
Last Updated on STN: 12 Feb 2002

AB The invention provides **Histidine Kinase** polypeptides and polynucleotides encoding **Histidine Kinase** polypeptides and methods for producing such polypeptides by **recombinant** techniques. Also provided are methods for utilizing **Histidine Kinase** polypeptides or polynucleotides to screen for antibacterial compounds.

L8 ANSWER 38 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:814336 HCAPLUS
DOCUMENT NUMBER: 133:359212
TITLE: **Staphylococcus aureus** two-component signal transduction **histidine kinase**-related 509HK proteins and polynucleotides for screening of antibacterial agents
INVENTOR(S): Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.; Biswas, Sanjoy; Throup, John P.; Burnham, Martin K. R.
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067783	A1	20001116	WO 2000-US11917	20000503
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6406889	B1	20020618	US 2000-564954	20000504

PRIORITY APPLN. INFO.: US 1999-132935P P 19990506
AB The invention provides S. aureus 509HK polypeptides and polynucleotides encoding 509HK polypeptides and methods for producing such polypeptides by **recombinant** techniques. Also provided are methods for utilizing 509HK polypeptides to screen for antibacterial compds.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 39 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:814249 HCAPLUS
DOCUMENT NUMBER: 133:359809
TITLE: **Cloning**, sequencing and **expression** of **Staphylococcus aureus histidine kinase** 0623HK and its therapeutic applications
INVENTOR(S): Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.; Biswas, Sanjoy; Throup, John P.; Burnham, Martin K. R.
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067575	A1	20001116	WO 2000-US12046	20000503
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1999-132759P P 19990506
AB The invention provides **histidine kinase** 0623HK and DNA sequences encoding 0623HK and methods for producing 0623HK by **recombinant** techniques. Also provided are methods for utilizing 0623HK to screen for antibacterial compds. In a further aspect, the invention relates to the uses of 0623HK in diagnostic assays for detecting diseases associated with microbial infections and conditions associated with

such infections. The 0623HK has protein sequence homol. with YesM polypeptide that may be a member of a two-component signal transduction **histidine kinase** family.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 58 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001284536 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11087872
TITLE: Rational design of a global inhibitor of the virulence response in **Staphylococcus aureus**, based in part on localization of the site of inhibition to the receptor-**histidine kinase**, AgrC.
AUTHOR: Lyon G J; Mayville P; Muir T W; Novick R P
CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.
CONTRACT NUMBER: AI 42783 (NIAID)
GM07739 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Nov 21) 97 (24) 13330-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524
AB Two-component signaling systems involving receptor-**histidine kinases** are ubiquitous in bacteria and have been found in yeast and plants. These systems provide the major means by which bacteria communicate with each other and the outside world. Remarkably, very little is known concerning the extracellular ligands that presumably bind to receptor-**histidine kinases** to initiate signaling. The two-component agr signaling circuit in **Staphylococcus aureus** is one system where the ligands are known in chemical detail, thus opening the door for detailed structure-activity relationship studies. These ligands are short (8- to 9-aa) peptides containing a thiolactone structure, in which the alpha-carboxyl group of the C-terminal amino acid is linked to the sulfhydryl group of a cysteine, which is always the fifth amino acid from the C terminus of the peptide. One unique aspect of the agr system is that peptides that activate virulence **expression** in one group of S. aureus strains also inhibit virulence **expression** in other groups of S. aureus strains. Herein, it is demonstrated by switching the receptor-**histidine kinase**, AgrC, between strains of different agr specificity types, that intragroup activation and intergroup inhibition are both mediated by the same group-specific receptors. These results have facilitated the development of a global inhibitor of virulence in S. aureus, which consists of a truncated version of one of the naturally occurring thiolactone peptides.

L8 ANSWER 41 OF 58 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2000100755 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10633099
TITLE: **Expression** of the multidrug resistance transporter NorA from **Staphylococcus aureus** is modified by a two-component regulatory system.
AUTHOR: Fournier B; Aras R; Hooper D C
CORPORATE SOURCE: Infectious Disease Division and Medical Services, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114-2696, USA.

CONTRACT NUMBER: AI23988 (NIAID)
SOURCE: Journal of bacteriology, (2000 Feb) 182 (3) 664-71.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000210

AB To dissect genetically the regulation of NorA, a multidrug transporter of **Staphylococcus aureus**, we analyzed the differential **expression** of the norA promoter using a transcriptional fusion with a beta-lactamase reporter gene. **Expression** studies with an arlS mutant revealed that the norA promoter is ArlS dependent. The arlR-arlS locus was shown to code for a two-component regulatory system. The protein ArlR has strong similarity to response regulators, and ArlS has strong similarity to protein **histidine kinases**.
We have also analyzed the 350-bp region upstream of the Shine-Dalgarno sequence of norA by gel mobility shift experiments. It was shown that only the 115-bp region upstream of the promoter was necessary for multiple binding of an 18-kDa protein. From transcriptional fusions, we have localized four different putative boxes of 6 bp, which appear to play a role in the binding of the 18-kDa protein and in the up-regulation of norA **expression** in the presence of the arlS mutation. Furthermore, the gel mobility shift of the 18-kDa protein was modified in the presence of the arlS mutation, and the arlS mutation altered the growth-phase regulation of NorA. These results indicate that **expression** of norA is modified by a two-component regulatory system.

L8 ANSWER 42 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:147405 SCISEARCH
THE GENUINE ARTICLE: 285BF
TITLE: A genomic analysis of two-component signal transduction in Streptococcus pneumoniae
AUTHOR: Throup J P; Koretke K K; Bryant A P; Ingraham K A; Chalker A F; Ge Y G; Marra A; Wallis N G; Brown J R; Holmes D J; Rosenberg M; Burnham M K R (Reprint)
CORPORATE SOURCE: SMITHKLINE BEECHAM PHARMACEUT RES & DEV, ANTIINFECT RES, 1250 S COLLEGEVILLE RD, COLLEGEVILLE, PA 19426 (Reprint); SMITHKLINE BEECHAM PHARMACEUT RES & DEV, ANTIINFECT RES, COLLEGEVILLE, PA 19426; SMITHKLINE BEECHAM PHARMACEUT RES & DEV, BIOINFORMAT, COLLEGEVILLE, PA 19426
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR MICROBIOLOGY, (FEB 2000) Vol. 35, No. 3, pp. 566-576.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0950-382X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A genomics-based approach was used to identify the entire gene complement of putative two-component signal transduction systems (TCSTSs) in Streptococcus pneumoniae. A total of 14 open reading frames (ORFs) were identified as putative response regulators, 13 of which were adjacent to genes encoding probable **histidine kinases**, Both the **histidine kinase** and response regulator proteins were categorized into subfamilies on the basis of phylogeny, Through a systematic programme of mutagenesis, the importance of each novel TCSTS

was determined with respect to viability and pathogenicity. One TCSTS was identified that was essential for the growth of S. pneumoniae, This locus was highly homologous to the yycFG gene pair encoding the essential response regulator/**histidine kinase** proteins identified in Bacillus subtilis and **Staphylococcus aureus**, Separate deletions of eight other loci led in each case to a dramatic attenuation of growth in a mouse respiratory tract infection model, suggesting that these signal transduction systems are important for the in vivo adaptation and pathogenesis of S. pneumoniae, The identification of conserved TCSTSs important for both pathogenicity and viability in a Gram-positive pathogen highlights the potential of two-component signal transduction as a multicomponent target for antibacterial drug discovery.

L8 ANSWER 43 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:156175 HCAPLUS
DOCUMENT NUMBER: 133:115743
TITLE: Identification of the Up- and Down-Regulated Genes in Vancomycin-Resistant **Staphylococcus aureus** Strains Mu3 and Mu50 by cDNA Differential Hybridization Method
AUTHOR(S): Kuroda, Makoto; Kuwahara-Arai, Kyoko; Hiramatsu, Keiichi
CORPORATE SOURCE: Department of Bacteriology, Faculty of Medicine, Juntendo University, Bunkyo-ku, Tokyo, 113-8421, Japan
SOURCE: Biochemical and Biophysical Research Communications (2000), 269(2), 485-490
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We previously reported the first vancomycin-resistant **Staphylococcus aureus** (VRSA) clin. strain, Mu50, whose cell wall is remarkably thickened resulting from the activation of cell-wall synthesis. To explore the genetic basis for the vancomycin resistance, cDNA differential hybridization was performed using RNAs extracted from a set of closely related S. aureus strains with various levels of vancomycin susceptibilities. The strains were Mu3 (MIC = 2 μg/mL), Mu50 (MIC = 8 μg/mL), and a susceptible revertant of Mu50, Mu50ω (MIC = 0.5 μg/mL). In this study, we report identification of a novel response regulator, designated vraR (standing for vancomycin-resistance associated gene R) whose transcription was remarkably up-regulated in Mu3 and Mu50 as compared to Mu50ω. Exptl. over- **expression** of VraR in vancomycin-susceptible strain N315P raised vancomycin resistance of the strain. Also, the genes coding for fructose utilization, fatty acid metabolism, and two putative ATP-binding cassette (ABC) transporter genes were found to be up-regulated in Mu3 and Mu50. On the other hand, Protein A **expression** was suppressed in Mu50, as compared with Mu3 and Mu50ω. We consider that the response regulator vraR is one of the key regulators modulating the level of vancomycin-resistance in S. aureus. Presumed increased uptake of fructose and altered fatty acid metabolism may also contribute to vancomycin resistance by supplying more precursor metabolites for cell-wall synthesis. (c) 2000 Academic Press.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 12
ACCESSION NUMBER: 1999-12556 BIOTECHDS
TITLE: Novel **histidine-kinase** polynucleotides and polypeptides used to screen for antibacterial compounds; **recombinant histidine-kinase**, nucleic acid, antibody and antagonist used in disease diagnosis, therapy, gene therapy and nucleic acid vaccine

AUTHOR: Wallis N G; Shilling L K; Mooney J L; Debouck C; Zhong Y; Jaworski D D; Wang M; Throup J P
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA.
PATENT INFO: WO 9936508 22 Jul 1999
APPLICATION INFO: WO 1999-US610 12 Jan 1999
PRIORITY INFO: US 1998-6627 13 Jan 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1999-444390 [37]

AB A **Staphylococcus aureus histidine-kinase** (HK) nucleic acid (NA, I) and protein are claimed. (I) has a given 2,201 bp DNA sequence, is at least 70% identical to a NA that encodes a given 451 amino acid protein sequence, or encodes a protein at least 70% identical to that sequence. Also claimed is a NA at least 70% identical to a NA encoding a mature HK derived from S. aureus. Also covered are: a vector encoding (I); a host cell transformed by that vector; a means of producing HK by culturing that cell; an antibody specific to HK; an antagonist (A) that inhibits HK **expression** or activity; a means of treating disease using the HK or (A); a means of diagnosing disease related to HK **expression**; a means of identifying compounds that modify HK activity; a means of inducing an immune response using the HK or a vector encoding it; a NA at least 70% identical to a NA encoding a 219 amino acid protein sequence; a NA at least 70% identical to a 2,201 or 736 bp DNA sequence; a HK with a 451 amino acid protein sequence; and a protein at least 70% identical to that sequence. These can be used in disease diagnosis, therapy, drug screening, gene therapy and in a nucleic acid vaccine. (43pp)

L8 ANSWER 45 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 13
ACCESSION NUMBER: 1999-08025 BIOTECHDS
TITLE: New **Staphylococcus aureus histidine-kinase** (HK) polypeptide and polynucleotides, useful for screening for antibiotics and for diagnosis, prevention and treatment of Staphylococci infections;
recombinant enzyme production via vector-mediated gene transfer and **expression** in a bacterium, antisense, antibody and antagonist for gene therapy and nucleic acid vaccine
AUTHOR: Traini C M; Kosmatka A L; Shilling L K; Warren R L; Wallis N G
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: EP 911406 28 Apr 1999
APPLICATION INFO: EP 1998-305806 21 Jul 1998
PRIORITY INFO: US 1997-963901 4 Nov 1997; US 1997-54073 29 Jul 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1999-246418 [21]

AB A **Staphylococcus aureus histidine-kinase** (HK) (I), which is part of the 2 component signal transduction system and at least 70% identical to a fully defined 147 amino acid protein sequence, is new. Also claimed are: a polynucleotide (II) (DNA or RNA), which is at least 70% identical to (I) or the mature HK protein **expressed** in S. aureus WCUH-29 (NCIMB 40771); a vector containing (II); a host cell containing the vector; an antibody immunospecific for (I); an antagonist which inhibits the activity or **expression** of (I); and the production of (I). (I) and (II) may be useful for the diagnosis of the stage and type of infection caused by an organism with the HK gene and for the screening of compounds which affect the activity of the protein. Antagonists, i.e. antibacterial drugs, may be used to inhibit HK activity and agonists to enhance HK

activity. The products may also be used for gene therapy with antisense sequences and nucleic acid vaccines. The antibodies produced may be used for immunization to prevent disease. (39pp)

L8 ANSWER 46 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:421810 HCAPLUS
DOCUMENT NUMBER: 131:69294
TITLE: Staphylococcus histidine protein kinase gene espB and response regulator gene espA and methods for screening for antibacterial agents and for treating bacterial infections
INVENTOR(S): Benton, Bret; Malouin, Francois; Martin, Patrick K.; Schmid, Molly B.; Sun, Dongxu
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9932657	A1	19990701	WO 1997-US23912		19971223
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9859033	A1	19990712	AU 1998-59033		19971223
US 6514746	B1	20030204	US 1998-82077		19980520
PRIORITY APPLN. INFO.:			US 1995-3798P	P	19950915
			US 1995-9102P	P	19951222
			US 1996-713718	A2	19960913
			WO 1997-US23912	A	19971223

AB This disclosure describes isolated or purified DNA sequences, useful for the development of antibacterial agents, which contain the coding sequences of bacterial genes which encode the components of a two-component regulatory pair. It further describes isolated or purified DNA sequences which are portions of such bacterial genes, which are useful as probes to identify the presence of the corresponding gene or the presence of a bacteria containing that gene. Also described are hypersensitive mutant cells containing a mutant gene corresponding to any of the identified sequences and methods of screening for antibacterial agents using such hypersensitive cells. In addition it describes methods of treating bacterial infections by administering an antibacterial agent active against one of the identified targets, as well as pharmaceutical compns. effective in such treatments. The espAB operon of S. aureus was **cloned** and sequenced. Sequence homologies indicate that these two genes encode a histidine protein kinase-response regulator pair. A method for screening substances which inhibit the EspAB system is presented. This method comprises a wild-type S. aureus strain and a mutant S. aureus strain which has a temperature-sensitive mutation in the espAB operon. Since the espAB operon is essential for S. aureus growth, inhibitors of the mutant are potential antibacterial agents.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:219876 HCAPLUS
DOCUMENT NUMBER: 130:247875

TITLE: Polynucleotide and polypeptide sequences from **Staphylococcus aureus** **expressed** in infected tissue
INVENTOR(S): Lonetto, Michael Arthur; Warren, Patrick Vernon; Burnham, Martin Karl Russel
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham Plc
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 905243	A2	19990331	EP 1998-306185	19980803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2239817	AA	19990205	CA 1998-2239817	19980805
JP 11155586	A2	19990615	JP 1998-255927	19980805

PRIORITY APPLN. INFO.: US 1997-55387P P 19970805

AB The invention provides novel polypeptides and polynucleotides encoding such polypeptides from **Staphylococcus aureus** and methods for producing such polypeptides by **recombinant** techniques. Thus, 14 partial or full-length gene sequences and the deduced amino acid sequences of their encoded proteins are provided. Also provided are methods for utilizing such polypeptides to screen for antibacterial compds.

L8 ANSWER 48 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 14
ACCESSION NUMBER: 1998-11158 BIOTECHDS
TITLE: DNA encoding staphylococcal **histidine-kinase**; **Staphylococcus aureus** **recombinant** protein preparation, DNA probe, and antagonist, used as antibiotic or for infectious disease therapy, gene therapy or nucleic acid vaccine, etc.
AUTHOR: Wallis N G
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: EP 870831 14 Oct 1998
APPLICATION INFO: EP 1998-302776 8 Apr 1998
PRIORITY INFO: US 1997-43489 10 Apr 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-523158 [45]

AB A new DNA sequence has at least 70% identity to a DNA sequence encoding a specified 363 amino acid protein sequence. Also claimed are: cDNA and DNA with at least 15 contiguous nucleotides of the new sequence (DNA probe); a **Staphylococcus aureus** WCUH 29 (NCIMB 40771) DNA sequence encoding **histidine-kinase**; a vector containing the DNA; a host cell containing the vector; producing the protein using the host cell; an antibody against the protein; and an antagonist which inhibits activity of the protein. The DNA and protein may be used for infectious disease diagnosis, therapy or gene therapy, in a **recombinant** vaccine or a nucleic acid vaccine, or for drug screening. Diseases associated with **expression** of the protein include otitis media, empyema, infective endocarditis, secretory diarrhea, cerebral abscess, blepharitis, perinephric abscess, impetigo or osteomyelitis, etc. Antibodies may be used as antibiotics. (30pp)

L8 ANSWER 49 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN

DUPLICATE 15
ACCESSION NUMBER: 1998-10739 BIOTECHDS
TITLE: New DNA encoding **Staphylococcus aureus histidine-kinase** used to prevent, treat, diagnose and vaccinate;
against respiratory tract infection, cardiac, gastrointestinal, central nervous system, eye, kidney, urinary tract, skin, bone and joint disorder
AUTHOR: Wallis N G
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: EP 863208 9 Sep 1998
APPLICATION INFO: EP 1998-301167 17 Feb 1998
PRIORITY INFO: US 1997-39478 25 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-458839 [40]
AB An isolated 2,700 bp nucleic acid (A) with at least 70% identity to a nucleic acid encoding an 861 amino acid protein (B), of given sequence, is claimed. Also claimed are nucleic acids complementary to (A), and partial sequences of (A). (A) encodes the mature **histidine-kinase** protein **expressed** by the gene NCIMB 40771. The claims also cover a vector containing (A), and a host cell transformed by that vector. Also covered are: the protein (B), a protein at least 70% identical to (B), an antibody (Ab) specific to (B), and an antagonist that inhibits (B)'s activity. The claims extend to a nucleic acid that can be obtained by screening a library containing a complete (A) under stringent conditions, and using a DNA probe with at least a partial sequence of (A). This is of use in treating an individual in need of **histidine-kinase**. Either the protein, or the DNA encoding it can be delivered. Alternatively the antagonist of (B) can be used to inhibit **histidine-kinase**. (A) can also be used to diagnose diseases related to (B) **expression**. (B) can be used to induce an immune response, causing production of (B)-Ab. (31pp)

L8 ANSWER 50 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 16
ACCESSION NUMBER: 1998-09561 BIOTECHDS
TITLE: New DNA encoding **Staphylococcus aureus histidine-kinase**;
used to screen compounds for antibiotic activity and as vaccines and to treat Staphylococcus infection in e.g. wounds and protheses
AUTHOR: Wallis N G; Shilling L K; Warren R L
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, Middlesex, UK.
PATENT INFO: EP 857787 12 Aug 1998
APPLICATION INFO: EP 1998-300829 4 Feb 1998
PRIORITY INFO: US 1997-37856 7 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-416009 [36]
AB An isolated DNA sequence (I) is claimed having at least 70% identity to a sequence encoding a 139 amino acid protein (II) (also claimed). Also claimed are: an isolated DNA sequence with at least 70% identity to a sequence encoding the same protein **expressed** by the **histidine-kinase** gene in **Staphylococcus aureus** WCUH29; a sequence encoding a protein whose sequence is at least 70% identical to (II); a DNA sequence complementary to (I); a vector comprising (I) and a host cell comprising this; a protein at least 70% identical to (II); antibody against (II); and an antagonist inhibiting the activity/**expression** of (II). (II) is used to treat an individual requiring **histidine-kinase**. The

antagonist can be used to inhibit it. (II) can also be used to diagnose disease related to **expression** or activity of (II) and as vaccines for and to treat **Staphylococcus aureus** infections. (I) and (II) are used to screen for compounds with antibiotic activity. They are also used in surgery and to treat wounds, and are also possible prophylactic antibiotics to prevent late deep infection after insertion of a prosthesis. (23pp)

L8 ANSWER 51 OF 58 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 1998294055 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9632266
TITLE: Transmembrane topology and histidine protein kinase activity of AgrC, the agr signal receptor in **Staphylococcus aureus**.
AUTHOR: Lina G; Jarraud S; Ji G; Greenland T; Pedraza A; Etienne J; Novick R P; Vandenesch F
CORPORATE SOURCE: UPRES EA1655, Faculte de Medecine Laennec, Lyon, France.. geralina@univ-lyon1.fr
SOURCE: Molecular microbiology, (1998 May) 28 (3) 655-62. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980924

AB The agr P2 operon in **Staphylococcus aureus** codes for the elements of a density-sensing cassette made up of a typical two-component signalling system and its corresponding inducer. It is postulated that the autoinducer, a post-translationally modified octapeptide generated from the AgrD peptide, interacts with a receptor protein, coded by agrC, to transmit a signal via AgrA regulating **expression** of staphylococcal virulence genes through **expression** of agr RNA III. We show by analysis of PhoA fusions that AgrC is a transmembrane protein, and confirm using Western blotting that a 46 kDa protein corresponding to AgrC is present in the bacterial membrane. This protein is autophosphorylated on a histidine residue only in response to supernatants from an agr+ strain, and can also respond to the purified native octapeptide. A **recombinant** fusion protein where most of the N-terminal region of AgrC is replaced by the Escherichia coli maltose-binding protein is also autophosphorylated in response to stimulation by agr+ supernatants or purified octapeptide. We conclude that AgrC is the sensor molecule of a typical two-component signal system in S. aureus, and that the ligand-binding site of AgrC is probably located in the third extracellular loop of the protein.

L8 ANSWER 52 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1998:927981 SCISEARCH
THE GENUINE ARTICLE: 143UN
TITLE: Evidence for common sites of contact between the antisigma factor SpoIIAB and its partners SpoIIAA and the developmental transcription factor sigma(F) in Bacillus subtilis
AUTHOR: Garsin D A; Paskowitz D M; Duncan L; Losick R (Reprint)
CORPORATE SOURCE: HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, 16 DIVERS AVE, CAMBRIDGE, MA 02138 (Reprint); HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, CAMBRIDGE, MA 02138
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (4 DEC 1998) Vol. 284, No. 3, pp. 557-568.
Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1

7DX, ENGLAND.
ISSN: 0022-2836.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The activity of the developmental transcription factor sigma(F) in Bacillus subtilis is governed by a switch involving the dual function protein SpoIIAB. SpoIIAB is an antisigma factor that forms complexes with sigma(F) and with an alternative partner protein SpoIIAA. SpoIIAB is also a protein kinase that can inactivate SpoIIAA by phosphorylating it on a serine residue. We sought to identify amino acids in SpoIIAB that are involved in the formation of the SpoIIAB-SpoIIAA complex by screening for mutants that were defective in the activation of sigma(F). This genetic screen, in combination with biochemical analysis and the construction of loss-of-sidechain (alanine substitution) mutants, led to the identification of amino acid side-chains in the N-terminal region of SpoIIAB that could contact SpoIIAA. Unexpectedly, the same amino acid side-chains (R20 and N50) that appear to touch SpoIIAA are required for binding to, and map represent sites of contact with, sigma(F). We propose that the N-terminal region of SpoIIAB forms a binding surface that is responsible for the formation of both the SpoIIAB-SpoIIAA and the SpoIIAB-sigma(F) complexes, and that in some cases the same amino acid side-chains contact both partner proteins. N50 is also the defining residue of a region of amino acid sequence homology known as the N-box that is shared by SpoIIAB and related serine protein kinases, as well as by members of a mechanistically dissimilar family of protein kinases that undergo autophosphorylation at a histidine residue. We discuss the implications of this finding for the mechanism of histidine autophosphorylation. (C) 1998 Academic Press.

L8 ANSWER 53 OF 58 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 1998294999 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9631538
TITLE: **Cloning** and characterization of an accessory gene regulator (agr)-like locus from Staphylococcus epidermidis.
AUTHOR: Van Wamel W J; van Rossum G; Verhoef J; Vandenbroucke-Grauls C M; Fluit A C
CORPORATE SOURCE: Eijkman-Winkler Institute for Microbiology, Infectious Diseases and Inflammation, Utrecht University, Netherlands.. w.j.b.vanwamel@lab.azu.nl
SOURCE: FEMS microbiology letters, (1998 Jun 1) 163 (1) 1-9. Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Z49220
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980709

AB The presence of sequences related to the agr of **Staphylococcus aureus** was demonstrated in Staphylococcus epidermidis by agr-specific PCR, and Southern blot. The agr-like locus of S. epidermidis A086 was **cloned** and sequenced. An overall homology of 68% was found between the agr locus from S. epidermidis and S. aureus. The agr locus from S. epidermidis was organized similar to those from S. aureus and S. lugdunensis. The putative RNAII molecule contains four open reading frames, agr A, B, C and D. AgrA was a response regulator. AgrB showed homology with transducer and translocase molecules. AgrC is expected to act as a histidine protein kinase in which a leucine zipper is present. AgrD is presumably processed into an autoinducer peptide. The

putative RNAIII molecule contained an open reading frame encoding a putative 26 amino acid (aa) polypeptide, which differed in 3 aa from the RNAIII encoded delta-toxin of S. aureus. Kinetic studies showed that the production of this RNAIII was elevated during the post-exponential phase. delta-Toxin activity was demonstrated for 21 of 23 tested S. epidermidis strains. Kinetic studies of the production of delta-toxin showed that the toxin was produced during the post-exponential phase. Sequencing of S. epidermidis A097, which showed a delayed agr-response, revealed a truncated AgrC lacking the **histidine kinase** domain.
These data indicate that an agr-like locus is active in S. epidermidis during the post-exponential phase.

L8 ANSWER 54 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1998:14702 SCISEARCH
THE GENUINE ARTICLE: YL836
TITLE: KapB is a lipoprotein required for KinB signal transduction and activation of the phosphorelay to sporulation in Bacillus subtilis
AUTHOR: Dartois V; Djavakhishvili T; Hoch J A (Reprint)
CORPORATE SOURCE: SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, 10550 N TORREY PINES RD, LA JOLLA, CA 92037 (Reprint); SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, LA JOLLA, CA 92037
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR MICROBIOLOGY, (DEC 1997) Vol. 26, No. 5, pp. 1097-1108.
Publisher: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL.
ISSN: 0950-382X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB KinB is one of the two major **histidine kinases** that provide phosphate input in the phosphorelay to produce SpoOA similar to P, the key transcription factor controlling the initiation of sporulation. A search for insertion mutants affected in activation of KinB-dependent sporulation led to the identification of the Igt locus encoding the lipoprotein glyceryltransferase required for the lipid modification of prolipoproteins before their cleavage and translocation across the cytoplasmic membrane. In parallel, a putative lipoprotein signal peptide cleavage site was detected in KapB, known to be strictly required for KinB-mediated sporulation and located downstream of KinB in a single transcription unit. Using PhoA peptide fusions, we have shown that KapB signal-peptide can direct active alkaline phosphatase to the outer surface of the cytoplasmic membrane in an LGT-dependent manner, strongly suggesting that KapB is a lipoprotein tethered to the outer face of the cytoplasmic membrane via a lipid anchor. As KapB proved to be dispensable for **expression** of the kinBkapB operon, a chimeric kinase was built consisting of KinA sensor domain fused to KinB kinase domain (KinA'-'B) to assess (i) the involvement of KapB in catalysis of the kinase reaction, and (ii) the ability of KinB to phosphorylate SpoOF in vitro. It was shown that KapB is dispensable for both in vivo and in vitro activation of the phosphorelay by the KinA'-'B chimera and that KinA'-'B phosphorylates SpoOF directly in vitro, Models for the role of KapB in regulating KinB activity are discussed.

L8 ANSWER 55 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 95:267936 SCISEARCH
THE GENUINE ARTICLE: QR556
TITLE: THE GENES INVOLVED IN PRODUCTION OF AND IMMUNITY TO

SAKACIN-A, A BACTERIOCIN FROM LACTOBACILLUS-SAKE LB706
AUTHOR: AXELSSON L (Reprint); HOLCK A
CORPORATE SOURCE: NORWEGIAN FOOD RES INST, MATFORSK, OSLOVEIEN 1, N-1430 AS, NORWAY (Reprint)
COUNTRY OF AUTHOR: NORWAY
SOURCE: JOURNAL OF BACTERIOLOGY, (APR 1995) Vol. 177, No. 8, pp. 2125-2137.
ISSN: 0021-9193.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 56
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sakacin A is a small, heat-stable, antilisterial bacteriocin produced by Lactobacillus sake Lb706. The nucleotide sequence of a 8,668-bp fragment, shown to contain all information necessary for sakacin A production and immunity, was determined. The sequence revealed the presence of two divergently transcribed operons. The first encompassed the structural gene sapA (previously designated sakA) and saiA, which encoded a putative peptide of 90 amino acid residues. The second encompassed sapK (previously designated sakB), sapR, sapT, and sapE, sapK and sapR presumably encoded a **histidine kinase** and a response regulator with marked similarities to the AgrB/AgrA type of two-component signal-transducing systems, The putative SapT and SapE proteins shared similarity,vith the Escherichia coli hemolysin A-like signal, sequence-independent transport systems, SapT was the HlyB analog with homology to bacterial ATP-binding cassette exporters implicated in bacteriocin transport. Frameshift mutations and deletion analyses showed that sapK and sapR were necessary for both production and immunity, whereas sapT and sapE were necessary for production but not for immunity. The putative SaiA peptide was shown to be involved in the immunity to sakacin A. The region between the operons contained IS1163, a recently described L. sake insertion element, IS1163 did not appear to be involved in **expression** of the sap genes, Northern (RNA) blot analysis revealed that the putative SapK/SapR system probably acts as a transcriptional activator on both operons. A 35-bp sequence, present upstream of the putative sapA promoter, and a similar sequence (30 of 35 nucleotides identical) upstream of sapK were shown to be necessary for proper **expression** and could thus be possible targets for transcriptional activation.

L8 ANSWER 56 OF 58 MEDLINE on STN
ACCESSION NUMBER: 94161498 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8117074
TITLE: The gene encoding plantaricin A, a bacteriocin from Lactobacillus plantarum C11, is located on the same transcription unit as an agr-like regulatory system.
AUTHOR: Diep D B; Havarstein L S; Nissen-Meyer J; Nes I F
CORPORATE SOURCE: Laboratory of Microbial Gene Technology, Agricultural University of Norway, As.
SOURCE: Applied and environmental microbiology, (1994 Jan) 60 (1) 160-6.
Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X75323
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 19950206
Entered Medline: 19940328

AB Purification and amino acid sequencing of plantaricin A, a bacteriocin from Lactobacillus plantarum C11, revealed that maximum bacteriocin

activity is associated with the complementary action of two almost-identical peptides, alpha and beta (J. Nissen-Meyer, A. G. Larsen, K. Sletten, M. Daeschel, and I. F. Nes, J. Gen. Microbiol. 139:1973-1978, 1993). A 5-kb chromosomal HindIII restriction fragment containing the structural gene of plantaricin A was **cloned** and sequenced. Only one gene encoding plantaricin A was found. The gene, termed plnA, encodes a 48-amino-acid precursor peptide, of which the 22 and 23 C-terminal amino acids correspond to the purified peptides. Northern (RNA) blot analysis demonstrated that a probe complementary to the coding strand of the plantaricin A gene hybridized to a 3.3-kb mRNA transcript. Further analysis of the 3.3-kb transcript demonstrated that it contains three additional open reading frames (plnB, plnC and plnD) downstream of plnA. The DNA sequences of plnB, plnC, and plnD revealed that their products closely resemble members of bacterial two-component signal transduction systems. The strongest homology was found to the accessory gene regulatory (agr) system, which controls **expression** of exoproteins during post-exponential growth in **Staphylococcus aureus**. The finding that plnABCD are transcribed from a common promoter suggests that the biological role played by the bacteriocin is somehow related to the regulatory function of the two-component system located on the same operon.

L8 ANSWER 57 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1994:191537 BIOSIS
DOCUMENT NUMBER: PREV199497204537
TITLE: Identification of a two-component regulatory system in **Staphylococcus aureus** that controls the **expression** of surface components.
AUTHOR(S): Bayles, Kenneth W.
CORPORATE SOURCE: UMBC, Baltimore, MD 21228, USA
SOURCE: Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18 PART A, pp. 44.
Meeting Info.: Keystone Symposium on Molecular Events in Microbial Pathogenesis. Santa Fe, New Mexico, USA. January 8-14, 1994.
ISSN: 0733-1959.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 1994
Last Updated on STN: 3 May 1994

L8 ANSWER 58 OF 58 MEDLINE on STN

ACCESSION NUMBER: 94028916 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8215360
TITLE: **Cloning** and nucleotide sequence of a gene from Lactobacillus sake Lb706 necessary for sakacin A production and immunity.
AUTHOR: Axelsson L; Holck A; Birkeland S E; Aukrust T; Blom H
CORPORATE SOURCE: MATFORSK, Norwegian Food Research Institute, As.
SOURCE: Applied and environmental microbiology, (1993 Sep) 59 (9) 2868-75.
Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X62978; GENBANK-X62979; GENBANK-X62980; GENBANK-X62981; GENBANK-X62986; GENBANK-X62987; GENBANK-X62988; GENBANK-X62989; GENBANK-X62990; GENBANK-Z21855
ENTRY MONTH: 199311

ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19950206
Entered Medline: 19931110

AB Sakacin A is an antilisterial bacteriocin produced by Lactobacillus sake Lb706. In order to identify genes involved in sakacin A production and immunity, the plasmid fraction of L. sake Lb706 was shotgun **cloned** directly into a sakacin A-nonproducing and -sensitive variant, L. sake Lb706-B, by using the broad-host-range vector pVS2. Two **clones** that produced sakacin A and were immune to the bacteriocin were obtained. A DNA fragment of approximately 1.8 kb, derived from a 60-kb plasmid of strain Lb706 and present in the inserts of both **clones**, was necessary for restoration of sakacin A production and immunity in strain Lb706-B. The sequence of the 1.8-kb fragment from one of the **clones** was determined. It contained one large open reading frame, designated sakB, potentially encoding a protein of 430 amino acid residues. Hybridization and nucleotide sequence analyses revealed that the **cloned** sakB complemented a mutated copy of sakB present in strain Lb706-B. The sakB gene mapped 1.6 kb from the previously **cloned** structural gene for sakacin A (sakA) on the 60-kb plasmid. The putative SakB protein shared 22% amino acid sequence identity (51% similarity if conservative changes are considered) to AgrB, the deduced amino acid sequence of the **Staphylococcus aureus** gene agrB. The polycistronic agr (accessory gene regulator) locus is involved in the regulation of exoprotein synthesis in S. aureus. Similar to the AgrB protein, SakB had some features in common with a family of transmembrane histidine protein kinases, involved in various adaptive response systems of bacteria.(ABSTRACT TRUNCATED AT 250 WORDS)

```
=> e wallis n g/au
E1            4     WALLIS N A/AU
E2           22     WALLIS N E/AU
E3          119 --> WALLIS N G/AU
E4            5     WALLIS N J/AU
E5            2     WALLIS N J H/AU
E6            1     WALLIS N R/AU
E7           15     WALLIS N T/AU
E8            2     WALLIS N Z/AU
E9            2     WALLIS NEIL R/AU
E10           1     WALLIS NG/AU
E11          16     WALLIS NICOLA/AU
E12          66     WALLIS NICOLA G/AU

=> s e3
L9          119 "WALLIS N G"/AU

=> e shilling l k/au
E1            1     SHILLING L A/AU
E2            1     SHILLING L J/AU
E3           28 --> SHILLING L K/AU
E4            8     SHILLING L M/AU
E5            1     SHILLING LILLESS MCPHERSON/AU
E6            4     SHILLING LISA/AU
E7           21     SHILLING LISA K/AU
E8           30     SHILLING LISA KATHLEEN/AU
E9            1     SHILLING LISA KETHLEEN/AU
E10           1     SHILLING LYNNDON/AU
E11          13     SHILLING M/AU
E12           1     SHILLING M A/AU

=> s e3-e9
L10          93 ("SHILLING L K"/AU OR "SHILLING L M"/AU OR "SHILLING LILLESS
                MCPHERSON"/AU OR "SHILLING LISA"/AU OR "SHILLING LISA K"/AU OR
                "SHILLING LISA KATHLEEN"/AU OR "SHILLING LISA KETHLEEN"/AU)
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```
=> e mooney j l/au
E1          16      MOONEY J K/AU
E2           5      MOONEY J K JR/AU
E3          63 --> MOONEY J L/AU
E4          39      MOONEY J M/AU
E5           1      MOONEY J MATTHEW/AU
E6          17      MOONEY J P/AU
E7          48      MOONEY J R/AU
E8           5      MOONEY J ROBERT/AU
E9          49      MOONEY J S/AU
E10         30      MOONEY J W/AU
E11          4      MOONEY JAMES/AU
E12          1      MOONEY JAMES A/AU

=> s e3
L11         63 "MOONEY J L"/AU

=> e debouck c/au
E1           1      DEBOUCHET J/AU
E2           6      DEBOUCHONY E T/AU
E3         416 --> DEBOUCK C/AU
E4          30      DEBOUCK C M/AU
E5           1      DEBOUCK C M */AU
E6         135      DEBOUCK CHRISTINE/AU
E7          19      DEBOUCK CHRISTINE M/AU
E8          11      DEBOUCK CHRISTINE MARIE/AU
E9           4      DEBOUCK D/AU
E10         47      DEBOUCK D G/AU
E11         12      DEBOUCK DANIEL G/AU
E12          2      DEBOUCK FERDINAND/AU

=> s e3
L12        416 "DEBOUCK C"/AU

=> s e3-e8
L13        612 ("DEBOUCK C"/AU OR "DEBOUCK C M"/AU OR "DEBOUCK C M *"/AU OR
               "DEBOUCK CHRISTINE"/AU OR "DEBOUCK CHRISTINE M"/AU OR "DEBOUCK
               CHRISTINE MARIE"/AU)

=> e zhong y y/au
E1          44      ZHONG Y W/AU
E2          53      ZHONG Y X/AU
E3          40 --> ZHONG Y Y/AU
E4          25      ZHONG Y Z/AU
E5           4      ZHONG YA/AU
E6           1      ZHONG YA LAN/AU
E7           8      ZHONG YA LING/AU
E8           6      ZHONG YA ZHEN/AU
E9           1      ZHONG YAFENG/AU
E10          2      ZHONG YAJUN/AU
E11          7      ZHONG YALAN/AU
E12          1      ZHONG YALI/AU

=> s e3
L14         40 "ZHONG Y Y"/AU

=> e jaworski d d/au
E1           3      JAWORSKI D A/AU
E2          75      JAWORSKI D C/AU
E3          87 --> JAWORSKI D D/AU
E4          59      JAWORSKI D M/AU
E5           1      JAWORSKI DALPHNE/AU
E6           1      JAWORSKI DD/AU
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E7            9     JAWORSKI DEBORAH/AU
E8           21     JAWORSKI DEBORAH C/AU
E9           64     JAWORSKI DEBORAH D/AU
E10          34     JAWORSKI DEBORAH DEE/AU
E11          21     JAWORSKI DIANE M/AU
E12           2     JAWORSKI DON/AU

=> s e3-e10
L15         276 ("JAWORSKI D D"/AU OR "JAWORSKI D M"/AU OR "JAWORSKI DALPHNE"/AU
                 OR "JAWORSKI DD"/AU OR "JAWORSKI DEBORAH"/AU OR "JAWORSKI DEBOR
                AH C"/AU OR "JAWORSKI DEBORAH D"/AU OR "JAWORSKI DEBORAH DEE"/AU
                )

=> e wang m/au
E1            1     WANG LYNN HUANG/AU
E2            1     WANG LYUAN/AU
E3         6684 --> WANG M/AU
E4           29     WANG M A/AU
E5          279     WANG M B/AU
E6         1168     WANG M C/AU
E7            2     WANG M C C/AU
E8            5     WANG M C H/AU
E9            1     WANG M C M/AU
E10           1     WANG M C T/AU
E11           2     WANG M C W/AU
E12         303     WANG M D/AU

=> s e3
L16        6684 "WANG M"/AU

=> e throup j p/au
E1           13     THROUP J/AU
E2            1     THROUP J A/AU
E3           55 --> THROUP J P/AU
E4           19     THROUP JOHN/AU
E5            1     THROUP JOHN A/AU
E6           35     THROUP JOHN P/AU
E7            5     THROUP JOHN PETER/AU
E8            4     THROUPE P/AU
E9            3     THROUVALAS A/AU
E10          73     THROUVALAS N/AU
E11           4     THROUVALAS N A/AU
E12          14     THROUVALAS NICOLAS/AU

=> s e3-e7
L17         115 ("THROUP J P"/AU OR "THROUP JOHN"/AU OR "THROUP JOHN A"/AU OR
                "THROUP JOHN P"/AU OR "THROUP JOHN PETER"/AU)

=> d his

     (FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004
L1       1253188 S KINASE?
L2        182160 S HISTIDINE
L3          4732 S L1(A)L2
L4       6785689 S CLON? OR EXPRESS? OR RECOMBINANT
L5        249014 S STAPHYLOCOCCUS (A)AUREUS
L6           163 S L3 AND L5
L7           102 S L4 AND L6
L8            58 DUP REM L7 (44 DUPLICATES REMOVED)
                 E WALLIS N G/AU
L9           119 S E3
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                E SHILLING L K/AU
L10           93 S E3-E9
                E MOONEY J L/AU
L11           63 S E3
                E DEBOUCK C/AU
L12          416 S E3
L13          612 S E3-E8
                E ZHONG Y Y/AU
L14           40 S E3
                E JAWORSKI D D/AU
L15          276 S E3-E10
                E WANG M/AU
L16         6684 S E3
                E THROUP J P/AU
L17          115 S E3-E7

=> s l8 or l9 or l10 or l11 or l13 or l14 or l15 or l16 or l17
L18        7894 L8 OR L9 OR L10 OR L11 OR L13 OR L14 OR L15 OR L16 OR
                L17

=> s l6 and l18
L19          72 L6 AND L18

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20          59 DUP REM L19 (13 DUPLICATES REMOVED)

=> d 1-59 ibib

L20  ANSWER 1 OF 59  SCISEARCH  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
ACCESSION NUMBER:    2004:517041  SCISEARCH
THE GENUINE ARTICLE: 824CT
TITLE:               Identification of a novel two-component system in
                     Streptococcus gordonii V288 involved in biofilm formation
AUTHOR:              Zhang Y S; Lei Y; Khammanivong A; Herzberg M C (Reprint)
CORPORATE SOURCE:    Univ Minnesota, Dept Oral Sci, 17-164 Moos Tower, 515
                     Delaware St SE, Minneapolis, MN 55455 USA (Reprint); Univ
                     Minnesota, Dept Oral Sci, Minneapolis, MN 55455 USA; Univ
                     Minnesota, Mucosal & Vaccine Res Ctr, Minneapolis, MN
                     55455 USA; Univ Minnesota, Sch Dent, Dept Oral Sci,
                     Minneapolis, MN 55455 USA
COUNTRY OF AUTHOR:   USA
SOURCE:              INFECTION AND IMMUNITY, (JUN 2004) Vol. 72, No. 6, pp.
                     3489-3494.
                     Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW,
                     WASHINGTON, DC 20036-2904 USA.
                     ISSN: 0019-9567.
DOCUMENT TYPE:       Article; Journal
LANGUAGE:            English
REFERENCE COUNT:     40
                    *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

L20  ANSWER 2 OF 59  SCISEARCH  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
ACCESSION NUMBER:    2004:498290  SCISEARCH
THE GENUINE ARTICLE: 822TE
TITLE:               Differential gene expression in response to
                     hydrogen peroxide and the putative PerR regulon of
                     Synechocystis sp strain PCC 6803
AUTHOR:              Li H; Singh A K; McIntyre L M; Sherman L A (Reprint)
CORPORATE SOURCE:    Purdue Univ, Dept Biol Sci, W Lafayette, IN 47907 USA
                     (Reprint); Purdue Univ, Dept Agron, W Lafayette, IN 47907
                     USA
```

COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BACTERIOLOGY, (JUN 2004) Vol. 186, No. 11, pp. 3331-3345.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0021-9193.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 75
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 3 OF 59 MEDLINE on STN
ACCESSION NUMBER: 2004166238 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15060046
TITLE: Characterization of virulence factor regulation by SrrAB, a two-component system in **Staphylococcus aureus**.
AUTHOR: Pragman Alexa A; Yarwood Jeremy M; Tripp Timothy J; Schlievert Patrick M
CORPORATE SOURCE: Department of Microbiology, University of Minnesota Medical School, Minneapolis, Minnesota 55455, USA.
CONTRACT NUMBER: T32 AI 07421 (NIAID)
SOURCE: Journal of bacteriology, (2004 Apr) 186 (8) 2430-8.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF260326
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040403
Last Updated on STN: 20040525
Entered Medline: 20040524

L20 ANSWER 4 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:271816 SCISEARCH
THE GENUINE ARTICLE: 802HO
TITLE: pbp2229-mediated nisin resistance mechanism in Listeria monocytogenes confers cross-protection to class IIa bacteriocins and affects virulence gene **expression**
AUTHOR: Gravesen A (Reprint); Kallipolitis B; Holmstrom K; Hoiby P E; Ramnath M; Knochel S
CORPORATE SOURCE: Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark (Reprint); Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, DK-1958 Frederiksberg C, Denmark; Univ So Denmark, Dept Biochem & Mol Biol, DK-5230 Odense, Denmark; Bioneer A S, Dept Mol Characterizat, DK-2970 Horsholm, Denmark; Univ Stellenbosch, Dept Biochem, ZA-7602 Matieland, South Africa
COUNTRY OF AUTHOR: Denmark; South Africa
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (MAR 2004) Vol. 70, No. 3, pp. 1669-1679.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0099-2240.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 5 OF 59 MEDLINE on STN

ACCESSION NUMBER: 2004212976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15109784
TITLE: Regulation of virulence determinants in **Staphylococcus aureus**: complexity and applications.
AUTHOR: Bronner Stephane; Monteil Henri; Prevost Gilles
CORPORATE SOURCE: Institut de Bacteriologie, Faculte de Medecine, Universite Louis Pasteur - Hopitaux, Universitaires de Strasbourg, 3, rue Koeberle, F-67000 Strasbourg, France.
SOURCE: FEMS microbiology reviews, (2004 May) 28 (2) 183-200. Ref: 114
Journal code: 8902526. ISSN: 0168-6445.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040428
Last Updated on STN: 20040703
Entered Medline: 20040702

L20 ANSWER 6 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:139965 SCISEARCH
THE GENUINE ARTICLE: 769FL
TITLE: Regulation of virulence determinants in vitro and in vivo in **Staphylococcus aureus**
AUTHOR: Cheung A L (Reprint); Bayer A S; Zhang G Y; Gresham H; Xiong Y Q
CORPORATE SOURCE: Dartmouth Coll Sch Med, Dept Microbiol, Hanover, NH 03755 USA (Reprint); Univ Calif Los Angeles, Harbor Med Ctr, Res & Educ Inst, Torrance, CA 90502 USA; Univ Calif Los Angeles, Sch Med, Los Angeles, CA 90024 USA; Natl Jewish Med & Res Ctr, Integrated Dept Immunol, Denver, CO 80206 USA; Univ New Mexico, Sch Med, Dept Microbiol & Mol Genet, Albuquerque, NM 87131 USA
COUNTRY OF AUTHOR: USA
SOURCE: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (15 JAN 2004) Vol. 40, No. 1, pp. 1-9.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0928-8244.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 53
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 7 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00275 BIOTECHDS
TITLE: New isolated nucleic acid encoding a peptide that kills both wild type pneumococci and a strain of Pneumococcus that is autolysin deficient, useful for treating or preventing bacterial infections or inflammations; **recombinant** protein production for use in disease therapy and drug screening
AUTHOR: NOVAK R; TUOMANEN E I
PATENT ASSIGNEE: ST JUDE CHILDREN'S RES HOSPITAL
PATENT INFO: US 6630583 7 Oct 2003
APPLICATION INFO: US 2000-493940 28 Jan 2000
PRIORITY INFO: US 2000-493940 28 Jan 2000; US 1998-84399 6 May 1998
DOCUMENT TYPE: Patent
LANGUAGE: English

OTHER SOURCE: WPI: 2003-810553 [76]

L20 ANSWER 8 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-18374 BIOTECHDS
TITLE: New oligonucleotide probes which specifically hybridize to **Staphylococcus aureus histidine kinase** essential genes, useful for developing antibacterial agents, or as probes for detecting the presence a particular gene;
drug screening for use in bacterium infection diagnosis and gene therapy
AUTHOR: BENTON B; MALOUIN F; MARTIN P K; SCHMID M B; SUN D
PATENT ASSIGNEE: ESSENTIAL THERAPEUTICS INC
PATENT INFO: US 6514746 4 Feb 2003
APPLICATION INFO: US 1998-82077 20 May 1998
PRIORITY INFO: US 1998-82077 20 May 1998; US 1995-3798 15 Sep 1995
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-478763 [45]

L20 ANSWER 9 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:1087573 SCISEARCH
THE GENUINE ARTICLE: 751GL
TITLE: Chemical communication among bacteria
AUTHOR: Taga M E; Bassler B L (Reprint)
CORPORATE SOURCE: Princeton Univ, Dept Mol Biol, Princeton, NJ 08544 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (25 NOV 2003) Vol. 100, Supp. [2], pp. 14549-14554.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 65
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 10 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:224073 SCISEARCH
THE GENUINE ARTICLE: 652DR
TITLE: Detection of secreted peptides by using hypothesis-driven multistage mass spectrometry
AUTHOR: Kalkum M; Lyon G J; Chait B T (Reprint)
CORPORATE SOURCE: Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem, 1230 York Ave, New York, NY 10021 USA (Reprint); Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem, New York, NY 10021 USA; Rockefeller Univ, Selma & Lawrence Ruben Lab Synthet Prot Chem, New York, NY 10021 USA
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (4 MAR 2003) Vol. 100, No. 5, pp. 2795-2800.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 53
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 11 OF 59 MEDLINE on STN
ACCESSION NUMBER: 2003570426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14651645
TITLE: Constitutive **expression** of PcsB suppresses the requirement for the essential VicR (YycF) response regulator in Streptococcus pneumoniae R6.
AUTHOR: Ng Wai-Leung; Robertson Gregory T; Kazmierczak Krystyna M; Zhao Jingyong; Gilmour Raymond; Winkler Malcolm E
CORPORATE SOURCE: Department of Biology, Indiana University, Jordan Hall 142, Bloomington, IN 47405, USA.
SOURCE: Molecular microbiology, (2003 Dec) 50 (5) 1647-63. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040302
Entered Medline: 20040301

L20 ANSWER 12 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:776164 HCAPLUS
DOCUMENT NUMBER: 139:359758
TITLE: Genes controlled by the essential YycG/YycF two-component system of Bacillus subtilis revealed through a novel hybrid regulator approach
AUTHOR(S): Howell, Alistair; Dubrac, Sarah; Andersen, Kasper Krogh; Noone, David; Fert, Juliette; Msadek, Tarek; Devine, Kevin
CORPORATE SOURCE: Department of Genetics, Smurfit Institute, Trinity College Dublin, Dublin, 2, Ire.
SOURCE: Molecular Microbiology (2003), 49(6), 1639-1655 CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:513309 SCISEARCH
THE GENUINE ARTICLE: 687GZ
TITLE: Autoinduction and signal transduction in the regulation of staphylococcal virulence
AUTHOR: Novick R P (Reprint)
CORPORATE SOURCE: NYU, Sch Med, Dept Microbiol, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA (Reprint); NYU, Sch Med, Dept Med, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR MICROBIOLOGY, (JUN 2003) Vol. 48, No. 6, pp. 1429-1449.
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
ISSN: 0950-382X.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 126
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 14 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-03939 BIOTECHDS

TITLE: Isolation and characterization of inhibitors of the essential **histidine kinase**, YycG in Bacillus subtilis and **Staphylococcus aureus**; vector-mediated gene transfer and **expression** in host cell for antibiotic screening and antibiotic-resistant bacterium infection therapy
AUTHOR: WATANABE T; HASHIMOTO Y; YAMAMOTO K; HIRAO K; ISHIHAMA A; HINO M; UTSUMI R
CORPORATE SOURCE: Kinki Univ; Nippon Inst Biol Sci; Fujisawa Pharmaceut Co Ltd
LOCATION: Utsumi R, Kinki Univ, Grad Sch Agr, Dept Biosci and Biotechnol, 3327-204 Nakamachi, Nara 6318505, Japan
SOURCE: JOURNAL OF ANTIBIOTICS; (2003) 56, 12, 1045-1052
ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English

L20 ANSWER 15 OF 59 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003448363 EMBASE
TITLE: Turning virulence on and off in Staphylococci.
AUTHOR: Muir T.W.
CORPORATE SOURCE: Dr. T.W. Muir, Lab. of Synthetic Protein Chemistry, The Rockefeller University, 1230 York Avenue, New York, NY 10021, United States. muirt@rockefeller.edu
SOURCE: Journal of Peptide Science, (2003) 9/10 (612-619).
Refs: 21
ISSN: 1075-2617 CODEN: JPSIEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L20 ANSWER 16 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:965696 HCAPLUS
DOCUMENT NUMBER: 139:194031
TITLE: Pathogenicity and **histidine kinases** : approaches toward the development of a new generation of antibiotics
AUTHOR(S): Hubbard, J.; Burnham, M. K. R.; **Throup, J. P.**
CORPORATE SOURCE: Computational and Structural Sciences, GlaxoSmithKline, Harlow, UK
SOURCE: Histidine Kinases in Signal Transduction (2003), 459-481. Editor(s): Inouye, Masayori; Dutta, Rinku. Elsevier Science: San Diego, Calif.
CODEN: 69DIUS; ISBN: 0-12-372484-8
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 59 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003373501 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12867749
TITLE: Biochemical characterization of the first essential two-component signal transduction system from **Staphylococcus aureus** and Streptococcus pneumoniae.
AUTHOR: Clausen Valerie A; Bae Weonhye; **Throup John**; Burnham Martin K R; Rosenberg Martin; Wallis Nicola G
CORPORATE SOURCE: Antimicrobials and Host Defense, GlaxoSmithKline Pharmaceuticals, Collegeville, PA, USA.
SOURCE: Journal of molecular microbiology and biotechnology, (2003)

5 (4) 252-60.
Journal code: 100892561. ISSN: 1464-1801.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030812
Last Updated on STN: 20030905
Entered Medline: 20030904

L20 ANSWER 18 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:517200 BIOSIS
DOCUMENT NUMBER: PREV200300519820
TITLE: Subcellular localization of SrrAB, a novel two-component regulatory system in **Staphylococcus aureus**.
AUTHOR(S): Pragman, A. A. [Reprint Author]; Schlievert, P. M. [Reprint Author]
CORPORATE SOURCE: University of Minnesota, Minneapolis, MN, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-066. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

L20 ANSWER 19 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:517239 BIOSIS
DOCUMENT NUMBER: PREV200300519832
TITLE: Two-component gene regulation in the biology of Enterococcus faecalis.
AUTHOR(S): Hancock, L. E. [Reprint Author]; Perego, M. [Reprint Author]
CORPORATE SOURCE: Scripps Research Institute, La Jolla, CA, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-078. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

L20 ANSWER 20 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-10378 BIOTECHDS
TITLE: Assay for detecting compounds that modulates **histidine kinase** activity, by contacting compound with kinase and substrate, and monitoring the rate or absolute amount of phosphate transfer by kinase to the substrate;
plasmid pMal-(RTM)-c2-mediated gene transfer and

expression in Escherichia coli for drug screening
AUTHOR: GOLDSCHMIDT R; LOELOFF M
PATENT ASSIGNEE: GOLDSCHMIDT R; LOELOFF M
PATENT INFO: US 2002004214 10 Jan 2002
APPLICATION INFO: US 1999-733731 21 Dec 1999
PRIORITY INFO: US 2000-733731 8 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-171025 [22]

L20 ANSWER 21 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:359080 SCISEARCH
THE GENUINE ARTICLE: 543NH
TITLE: rgf encodes a novel two-component signal transduction system of Streptococcus agalactiae
AUTHOR: Spellerberg B (Reprint); Rozdzinski E; Martin S; Weber-Heynemann J; Lutticken R
CORPORATE SOURCE: Univ Ulm, Dept Med Microbiol & Hyg, Robert Koch Str 8, D-89081 Ulm, Germany (Reprint); Univ Ulm, Dept Med Microbiol & Hyg, D-89081 Ulm, Germany; Univ Hosp Aachen, Inst Med Microbiol, D-52057 Aachen, Germany; Univ Hosp Aachen, Natl Reference Ctr Streptococci, D-52057 Aachen, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: INFECTION AND IMMUNITY, (MAY 2002) Vol. 70, No. 5, pp. 2434-2440.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 22 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:652704 SCISEARCH
THE GENUINE ARTICLE: 579BC
TITLE: Recent progress in Bacillus subtilis two-component regulation
AUTHOR: Ogura M; Tanaka T (Reprint)
CORPORATE SOURCE: Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci, Orido 3-20-1, Shizuoka 4248610, Japan (Reprint); Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci, Shizuoka 4248610, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: FRONTIERS IN BIOSCIENCE, (AUG 2002) Vol. 7, pp. D1815-D1824.
Publisher: FRONTIERS IN BIOSCIENCE INC, C/O NORTH SHORE UNIV HOSPITAL, BIOMEDICAL RESEARCH CENTER, 350 COMMUNITY DR, MANHASSET, NY 11030 USA.
ISSN: 1093-9946.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 77
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 23 OF 59 MEDLINE on STN
ACCESSION NUMBER: 2002080831 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11807070
TITLE: Repression of the **Staphylococcus aureus** accessory gene regulator in serum and in vivo.
AUTHOR: Yarwood Jeremy M; McCormick John K; Paustian Michael L;

Kapur Vivek; Schlievert Patrick M
CORPORATE SOURCE: Department of Microbiology, Medical School, University of Minnesota, Minneapolis, Minnesota, USA.
CONTRACT NUMBER: HL36611 (NHLBI)
SOURCE: Journal of bacteriology, (2002 Feb) 184 (4) 1095-101. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020128
Last Updated on STN: 20020320
Entered Medline: 20020319

L20 ANSWER 24 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:267761 BIOSIS
DOCUMENT NUMBER: PREV200200267761
TITLE: **Histidine kinases** as targets for new antimicrobial agents.
AUTHOR(S): Matsushita, Masayuki [Reprint author]; Janda, Kim D. [Reprint author]
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute and Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, BCC-582, La Jolla, CA, 92037, USA kdjanda@scripps.edu
SOURCE: Bioorganic and Medicinal Chemistry, (April, 2002) Vol. 10, No. 4, pp. 855-867. print. ISSN: 0968-0896.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002

L20 ANSWER 25 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:756564 SCISEARCH
THE GENUINE ARTICLE: 591TY
TITLE: Two-component and phosphorelay signal-transduction systems as therapeutic targets
AUTHOR: Stephenson K (Reprint); Hoch J A
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt Med, La Jolla, CA 92037 USA
COUNTRY OF AUTHOR: USA
SOURCE: CURRENT OPINION IN PHARMACOLOGY, (OCT 2002) Vol. 2, No. 5, pp. 507-512.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
ISSN: 1471-4892.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 63
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 26 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:858990 HCAPLUS
DOCUMENT NUMBER: 138:148485
TITLE: Regulatory relationship of two-component and ABC transport systems and clustering of their genes in the Bacillus/Clostridium group, suggest a functional link

between them
AUTHOR(S): Joseph, Pascale; Fichant, Gwennaele; Quentin, Yves; Denizot, Francois
CORPORATE SOURCE: Laboratoire de Chimie Bacterienne, Institut de Biologie Structurale et Microbiologie, CNRS 31, Marseille, 13402, Fr.
SOURCE: Journal of Molecular Microbiology and Biotechnology (2002), 4(5), 503-513
CODEN: JMMBFF; ISSN: 1464-1801
PUBLISHER: Horizon Scientific Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 27 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:602183 SCISEARCH
THE GENUINE ARTICLE: 571KL
TITLE: Virulence- and antibiotic resistance-associated two-component signal transduction systems of Gram-positive pathogenic bacteria as targets for antimicrobial therapy
AUTHOR: Stephenson K; Hoch J A (Reprint)
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, Div Cellular Biol, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt Med, Div Cellular Biol, La Jolla, CA 92037 USA
COUNTRY OF AUTHOR: USA
SOURCE: PHARMACOLOGY & THERAPEUTICS, (FEB-MAR 2002) Vol. 93, No. 2-3, pp. 293-305.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0163-7258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 92
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 28 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:613874 HCAPLUS
TITLE: Turning virulence on and off in Staphylococci
AUTHOR(S): Muir, Tom W.
CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, Rockefeller University, New York City, NY, 10021, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), BIOL-102. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

L20 ANSWER 29 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:452628 BIOSIS
DOCUMENT NUMBER: PREV200100452628
TITLE: **Histidine kinase** of **Staphylococcus aureus**.
AUTHOR(S): Wallis, Nicola Gail [Inventor]; Traini, Christopher Michael [Inventor]; Kosmatka, Anna Lisa [Inventor]; **Shilling, Lisa Kathleen** [Inventor]; Warren, Richard Lloyd [Inventor]
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation, Philadephia, PA, USA; SmithKline Beecham plc, Brenford, UK

PATENT INFORMATION: US 6270992 August 07, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 7, 2001) Vol. 1249, No. 1. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002

L20 ANSWER 30 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:378355 BIOSIS
DOCUMENT NUMBER: PREV200100378355
TITLE: **Histidine kinase**, 636 HK, of **staphylococcus aureus**.
AUTHOR(S): Burnham, Martin K R [Inventor]; Palmer, Leslie Marie [Inventor]; **Throup, John Peter** [Inventor, Reprint author]; Van Horn, Stephanie [Inventor]; Warren, Richard Lloyd [Inventor]
CORPORATE SOURCE: Royersford, PA, USA
ASSIGNEE: SmithKline Beecham Corporation
PATENT INFORMATION: US 6194174 February 27, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Aug 2001
Last Updated on STN: 19 Feb 2002

L20 ANSWER 31 OF 59 MEDLINE on STN
ACCESSION NUMBER: 2001469003 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11513618
TITLE: The srhSR gene pair from **Staphylococcus aureus**: genomic and proteomic approaches to the identification and characterization of gene function.
AUTHOR: **Throup J P**; Zappacosta F; Lunsford R D; Annan R S; Carr S A; Lonsdale J T; Bryant A P; McDevitt D; Rosenberg M; Burnham M K
CORPORATE SOURCE: Anti-infectives Research, GlaxoSmithKline Pharmaceuticals Research and Development, Collegeville, Pennsylvania 19426, USA.. John_Throup-1@sbphrd.com
SOURCE: Biochemistry, (2001 Aug 28) 40 (34) 10392-401. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010830
Last Updated on STN: 20030325
Entered Medline: 20010927

L20 ANSWER 32 OF 59 MEDLINE on STN
ACCESSION NUMBER: 2001337274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11136460
TITLE: Group A streptococcal growth phase-associated virulence factor regulation by a novel operon (Fas) with homologies to two-component-type regulators requires a small RNA molecule.
AUTHOR: Kreikemeyer B; Boyle M D; Buttaro B A; Heinemann M; Podbielski A
CORPORATE SOURCE: Department of Medical Microbiology and Hygiene, University Hospital Ulm, Robert-Koch-Str. 8, D-89081 Ulm, Germany.

SOURCE: Molecular microbiology, (2001 Jan) 39 (2) 392-406.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

L20 ANSWER 33 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:455510 HCAPLUS
DOCUMENT NUMBER: 135:192773
TITLE: Characterization of bacteriocin N15 produced by Enterococcus faecium N15 and **cloning** of the related genes
AUTHOR(S): Losteinkit, Chanvadee; Uchiyama, Keiji; Ochi, Shuichiro; Takaoka, Tomoyo; Nagahisa, Keisuke; Shioya, Suteaki
CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Osaka University, Suita, 565-0871, Japan
SOURCE: Journal of Bioscience and Bioengineering (2001), 91(4), 390-395
CODEN: JBBIF6; ISSN: 1389-1723
PUBLISHER: Society for Bioscience and Bioengineering, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 34 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 2
ACCESSION NUMBER: 2001-03236 BIOTECHDS
TITLE: **Histidine-kinase** polypeptides and polynucleotides, useful for treating bacterial infections caused by **Staphylococcus aureus** such as otitis media, thyroiditis, empyema and for screening antibacterial compounds;
the use of **recombinant histidine-kinase**
AUTHOR: **Throup J P**; Palmer L M; Burnham M K; Warren R L; van Horn S
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: WO 2000068360 16 Nov 2000
APPLICATION INFO: WO 2000-US12862 11 May 2000
PRIORITY INFO: US 1999-310275 12 May 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-016089 [02]

L20 ANSWER 35 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:239703 BIOSIS
DOCUMENT NUMBER: PREV200100239703
TITLE: Sensor **histidine kinase** of **Staphylococcus Aureus**.
AUTHOR(S): Wallis, Nicola Gail [Inventor]
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation
PATENT INFORMATION: US 6127147 October 03, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 3, 2000) Vol. 1239, No. 1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2001
Last Updated on STN: 18 Feb 2002

L20 ANSWER 36 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:70585 BIOSIS
DOCUMENT NUMBER: PREV200100070585
TITLE: Sensor **histidine kinase** of **Staphylococcus aureus**.
AUTHOR(S): Wallis, Nicola Gail [Inventor]
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation; SmithKline Beecham, p.l.c., UK
PATENT INFORMATION: US 6071894 June 06, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 6, 2000) Vol. 1235, No. 1. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Feb 2001
Last Updated on STN: 12 Feb 2002

L20 ANSWER 37 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2001-00945 BIOTECHDS
TITLE: **Histidine-kinase** family polypeptides obtained from **Staphylococcus aureus**, useful for developing antibacterial compounds; vector-mediated gene transfer and **expression** in host cell, antibody, agonist and antagonist, appl. cancer and bacterium infection therapy
AUTHOR: **Wallis N G**
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA.
PATENT INFO: WO 2000056865 28 Sep 2000
APPLICATION INFO: WO 2000-US6206 9 Mar 2000
PRIORITY INFO: US 1999-274058 22 Mar 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-638259 [61]

L20 ANSWER 38 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2001-00532 BIOTECHDS
TITLE: New **histidine-kinase** polypeptide and polynucleotide, useful for treating, preventing or diagnosing microbial diseases, especially infections caused by **Staphylococcus aureus**, e.g. otitis media, thyroiditis or wound infection; vector-mediated gene transfer and **expression** in host cell, antibody, agonist and antagonist
AUTHOR: **Wallis N G**
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philladelphia, PA, USA.
PATENT INFO: WO 2000056154 28 Sep 2000
APPLICATION INFO: WO 2000-US6133 8 Mar 2000
PRIORITY INFO: US 1999-272414 19 Mar 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-611569 [58]

L20 ANSWER 39 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:814336 HCAPLUS
DOCUMENT NUMBER: 133:359212
TITLE: **Staphylococcus aureus**

two-component signal transduction **histidine kinase**-related 509HK proteins and polynucleotides for screening of antibacterial agents

INVENTOR(S): Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.; Biswas, Sanjoy; **Throup, John P.**; Burnham, Martin K. R.

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067783	A1	20001116	WO 2000-US11917	20000503
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6406889	B1	20020618	US 2000-564954	20000504

PRIORITY APPLN. INFO.: US 1999-132935P P 19990506

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 40 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:814249 HCAPLUS

DOCUMENT NUMBER: 133:359809

TITLE: **Cloning**, sequencing and **expression** of **Staphylococcus aureus histidine kinase** 0623HK and its therapeutic applications

INVENTOR(S): Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.; Biswas, Sanjoy; **Throup, John P.**; Burnham, Martin K. R.

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067575	A1	20001116	WO 2000-US12046	20000503
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1999-132759P P 19990506

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 41 OF 59 MEDLINE on STN

ACCESSION NUMBER: 2001284536 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11087872

TITLE: Rational design of a global inhibitor of the virulence response in **Staphylococcus aureus**, based in part on localization of the site of inhibition to the receptor-**histidine kinase**, AgrC.

AUTHOR: Lyon G J; Mayville P; Muir T W; Novick R P

CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, The Rockefeller

University, 1230 York Avenue, New York, NY 10021, USA.
CONTRACT NUMBER: AI 42783 (NIAID)
GM07739 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Nov 21) 97 (24) 13330-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

L20 ANSWER 42 OF 59 MEDLINE on STN
ACCESSION NUMBER: 2000100755 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10633099
TITLE: **Expression** of the multidrug resistance transporter NorA from **Staphylococcus aureus** is modified by a two-component regulatory system.
AUTHOR: Fournier B; Aras R; Hooper D C
CORPORATE SOURCE: Infectious Disease Division and Medical Services, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114-2696, USA.
CONTRACT NUMBER: AI23988 (NIAID)
SOURCE: Journal of bacteriology, (2000 Feb) 182 (3) 664-71. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000210

L20 ANSWER 43 OF 59 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2000138359 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10672179
TITLE: A genomic analysis of two-component signal transduction in Streptococcus pneumoniae.
AUTHOR: **Throup J P**; Koretke K K; Bryant A P; Ingraham K A; Chalker A F; Ge Y; Marra A; **Wallis N G**; Brown J R; Holmes D J; Rosenberg M; Burnham M K
CORPORATE SOURCE: Anti-infectives Research; Bioinformatics, SmithKline Beecham Pharmaceuticals Research and Development, 1250 S. Collegeville Road, Collegeville, PA 19426, USA.
SOURCE: Molecular microbiology, (2000 Feb) 35 (3) 566-76. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000328

L20 ANSWER 44 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:156175 HCAPLUS
DOCUMENT NUMBER: 133:115743
TITLE: Identification of the Up- and Down-Regulated Genes in

Vancomycin-Resistant **Staphylococcus aureus** Strains Mu3 and Mu50 by cDNA Differential Hybridization Method

AUTHOR(S): Kuroda, Makoto; Kuwahara-Arai, Kyoko; Hiramatsu, Keiichi

CORPORATE SOURCE: Department of Bacteriology, Faculty of Medicine, Juntendo University, Bunkyo-ku, Tokyo, 113-8421, Japan

SOURCE: Biochemical and Biophysical Research Communications (2000), 269(2), 485-490
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 45 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 4

ACCESSION NUMBER: 1999-12556 BIOTECHDS

TITLE: Novel **histidine-kinase** polynucleotides and polypeptides used to screen for antibacterial compounds; **recombinant histidine-kinase**, nucleic acid, antibody and antagonist used in disease diagnosis, therapy, gene therapy and nucleic acid vaccine

AUTHOR: **Wallis N G**; **Shilling L K**; **Mooney J L**; **Debouck C**; Zhong Y; **Jaworski D D**; **Wang M**; **Throup J P**

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA.

PATENT INFO: WO 9936508 22 Jul 1999

APPLICATION INFO: WO 1999-US610 12 Jan 1999

PRIORITY INFO: US 1998-6627 13 Jan 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1999-444390 [37]

L20 ANSWER 46 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 1999-08025 BIOTECHDS

TITLE: New **Staphylococcus aureus histidine-kinase** (HK) polypeptide and polynucleotides, useful for screening for antibiotics and for diagnosis, prevention and treatment of Staphylococci infections; **recombinant** enzyme production via vector-mediated gene transfer and **expression** in a bacterium, antisense, antibody and antagonist for gene therapy and nucleic acid vaccine

AUTHOR: Traini C M; Kosmatka A L; **Shilling L K**; Warren R L; **Wallis N G**

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, UK.

PATENT INFO: EP 911406 28 Apr 1999

APPLICATION INFO: EP 1998-305806 21 Jul 1998

PRIORITY INFO: US 1997-963901 4 Nov 1997; US 1997-54073 29 Jul 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1999-246418 [21]

L20 ANSWER 47 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:421810 HCAPLUS

DOCUMENT NUMBER: 131:69294

TITLE: Staphylococcus histidine protein kinase gene espB and response regulator gene espA and methods for screening

for antibacterial agents and for treating bacterial infections
INVENTOR(S): Benton, Bret; Malouin, Francois; Martin, Patrick K.; Schmid, Molly B.; Sun, Dongxu
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932657	A1	19990701	WO 1997-US23912	19971223
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9859033	A1	19990712	AU 1998-59033	19971223
US 6514746	B1	20030204	US 1998-82077	19980520
PRIORITY APPLN. INFO.:			US 1995-3798P	P 19950915
			US 1995-9102P	P 19951222
			US 1996-713718	A2 19960913
			WO 1997-US23912	A 19971223

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 48 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:219876 HCAPLUS
DOCUMENT NUMBER: 130:247875
TITLE: Polynucleotide and polypeptide sequences from **Staphylococcus aureus** **expressed** in infected tissue
INVENTOR(S): Lonetto, Michael Arthur; Warren, Patrick Vernon; Burnham, Martin Karl Russel
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline Beecham Plc
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 905243	A2	19990331	EP 1998-306185	19980803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2239817	AA	19990205	CA 1998-2239817	19980805
JP 11155586	A2	19990615	JP 1998-255927	19980805
PRIORITY APPLN. INFO.:			US 1997-55387P	P 19970805

L20 ANSWER 49 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 6
ACCESSION NUMBER: 1998-09561 BIOTECHDS
TITLE: New DNA encoding **Staphylococcus aureus** **histidine-kinase**;
used to screen compounds for antibiotic activity and as

vaccines and to treat Staphylococcus infection in e.g. wounds and protheses

AUTHOR: **Wallis N G**; **Shilling L K**; Warren R L
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, Middlesex, UK.
PATENT INFO: EP 857787 12 Aug 1998
APPLICATION INFO: EP 1998-300829 4 Feb 1998
PRIORITY INFO: US 1997-37856 7 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-416009 [36]

L20 ANSWER 50 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1998-11158 BIOTECHDS
TITLE: DNA encoding staphylococcal **histidine-kinase**;
Staphylococcus aureus **recombinant** protein preparation, DNA probe, and antagonist, used as antibiotic or for infectious disease therapy, gene therapy or nucleic acid vaccine, etc.
AUTHOR: **Wallis N G**
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: EP 870831 14 Oct 1998
APPLICATION INFO: EP 1998-302776 8 Apr 1998
PRIORITY INFO: US 1997-43489 10 Apr 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-523158 [45]

L20 ANSWER 51 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1998-10739 BIOTECHDS
TITLE: New DNA encoding **Staphylococcus aureus** **histidine-kinase** used to prevent, treat, diagnose and vaccinate;
against respiratory tract infection, cardiac, gastrointestinal, central nervous system, eye, kidney, urinary tract, skin, bone and joint disorder
AUTHOR: **Wallis N G**
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: EP 863208 9 Sep 1998
APPLICATION INFO: EP 1998-301167 17 Feb 1998
PRIORITY INFO: US 1997-39478 25 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-458839 [40]

L20 ANSWER 52 OF 59 MEDLINE on STN
ACCESSION NUMBER: 1998294055 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9632266
TITLE: Transmembrane topology and histidine protein kinase activity of AgrC, the agr signal receptor in **Staphylococcus aureus**.
AUTHOR: Lina G; Jarraud S; Ji G; Greenland T; Pedraza A; Etienne J; Novick R P; Vandenesch F
CORPORATE SOURCE: UPRES EA1655, Faculte de Medecine Laennec, Lyon, France.. geral'ina@univ-lyon1.fr
SOURCE: Molecular microbiology, (1998 May) 28 (3) 655-62. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980924

L20 ANSWER 53 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1998:927981 SCISEARCH
THE GENUINE ARTICLE: 143UN
TITLE: Evidence for common sites of contact between the antisigma factor SpoIIAB and its partners SpoIIAA and the developmental transcription factor sigma(F) in Bacillus subtilis
AUTHOR: Garsin D A; Paskowitz D M; Duncan L; Losick R (Reprint)
CORPORATE SOURCE: HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, 16 DIVERS AVE, CAMBRIDGE, MA 02138 (Reprint); HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, CAMBRIDGE, MA 02138
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (4 DEC 1998) Vol. 284, No. 3, pp. 557-568.
Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.
ISSN: 0022-2836.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 54 OF 59 MEDLINE on STN
ACCESSION NUMBER: 1998294999 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9631538
TITLE: **Cloning** and characterization of an accessory gene regulator (agr)-like locus from Staphylococcus epidermidis.
AUTHOR: Van Wamel W J; van Rossum G; Verhoef J; Vandenbroucke-Grauls C M; Fluit A C
CORPORATE SOURCE: Eijkman-Winkler Institute for Microbiology, Infectious Diseases and Inflammation, Utrecht University, Netherlands.. w.j.b.vanwamel@lab.azu.nl
SOURCE: FEMS microbiology letters, (1998 Jun 1) 163 (1) 1-9.
Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Z49220
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980709

L20 ANSWER 55 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1998:14702 SCISEARCH
THE GENUINE ARTICLE: YL836
TITLE: KapB is a lipoprotein required for KinB signal transduction and activation of the phosphorelay to sporulation in Bacillus subtilis
AUTHOR: Dartois V; Djavakhishvili T; Hoch J A (Reprint)
CORPORATE SOURCE: SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, 10550 N TORREY PINES RD, LA JOLLA, CA 92037 (Reprint); SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, LA JOLLA, CA 92037
COUNTRY OF AUTHOR: USA

SOURCE: MOLECULAR MICROBIOLOGY, (DEC 1997) Vol. 26, No. 5, pp. 1097-1108.
Publisher: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL.
ISSN: 0950-382X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 56 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 95:267936 SCISEARCH
THE GENUINE ARTICLE: QR556
TITLE: THE GENES INVOLVED IN PRODUCTION OF AND IMMUNITY TO SAKACIN-A, A BACTERIOCIN FROM LACTOBACILLUS-SAKE LB706
AUTHOR: AXELSSON L (Reprint); HOLCK A
CORPORATE SOURCE: NORWEGIAN FOOD RES INST, MATFORSK, OSLOVEIEN 1, N-1430 AS, NORWAY (Reprint)
COUNTRY OF AUTHOR: NORWAY
SOURCE: JOURNAL OF BACTERIOLOGY, (APR 1995) Vol. 177, No. 8, pp. 2125-2137.
ISSN: 0021-9193.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 56
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L20 ANSWER 57 OF 59 MEDLINE on STN
ACCESSION NUMBER: 94161498 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8117074
TITLE: The gene encoding plantaricin A, a bacteriocin from Lactobacillus plantarum C11, is located on the same transcription unit as an agr-like regulatory system.
AUTHOR: Diep D B; Havarstein L S; Nissen-Meyer J; Nes I F
CORPORATE SOURCE: Laboratory of Microbial Gene Technology, Agricultural University of Norway, As.
SOURCE: Applied and environmental microbiology, (1994 Jan) 60 (1) 160-6.
Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X75323
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 19950206
Entered Medline: 19940328

L20 ANSWER 58 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1994:191537 BIOSIS
DOCUMENT NUMBER: PREV199497204537
TITLE: Identification of a two-component regulatory system in **Staphylococcus aureus** that controls the **expression** of surface components.
AUTHOR(S): Bayles, Kenneth W.
CORPORATE SOURCE: UMBC, Baltimore, MD 21228, USA
SOURCE: Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18 PART A, pp. 44.
Meeting Info.: Keystone Symposium on Molecular Events in

Microbial Pathogenesis. Santa Fe, New Mexico, USA. January 8-14, 1994.
ISSN: 0733-1959.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 1994
Last Updated on STN: 3 May 1994

L20 ANSWER 59 OF 59 MEDLINE on STN
ACCESSION NUMBER: 94028916 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8215360
TITLE: **Cloning** and nucleotide sequence of a gene from Lactobacillus sake Lb706 necessary for sakacin A production and immunity.
AUTHOR: Axelsson L; Holck A; Birkeland S E; Aukrust T; Blom H
CORPORATE SOURCE: MATFORSK, Norwegian Food Research Institute, As.
SOURCE: Applied and environmental microbiology, (1993 Sep) 59 (9) 2868-75.
Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X62978; GENBANK-X62979; GENBANK-X62980; GENBANK-X62981; GENBANK-X62986; GENBANK-X62987; GENBANK-X62988; GENBANK-X62989; GENBANK-X62990; GENBANK-Z21855
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19950206
Entered Medline: 19931110

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(FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004

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L1      1253188 S KINASE?
L2       182160 S HISTIDINE
L3         4732 S L1(A)L2
L4      6785689 S CLON? OR EXPRESS? OR RECOMBINANT
L5       249014 S STAPHYLOCOCCUS (A)AUREUS
L6          163 S L3 AND L5
L7          102 S L4 AND L6
L8           58 DUP REM L7 (44 DUPLICATES REMOVED)
                E WALLIS N G/AU
L9          119 S E3
                E SHILLING L K/AU
L10          93 S E3-E9
                E MOONEY J L/AU
L11          63 S E3
                E DEBOUCK C/AU
L12         416 S E3
L13         612 S E3-E8
                E ZHONG Y Y/AU
L14          40 S E3
                E JAWORSKI D D/AU
L15         276 S E3-E10
                E WANG M/AU
L16        6684 S E3
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                E THROUP J P/AU
L17          115 S E3-E7
L18         7894 S L8 OR L9 OR L10 OR L11 OR L13 OR L14 OR L15 OR L16 OR L
L19           72 S L6 AND L18
L20           59 DUP REM L19 (13 DUPLICATES REMOVED)
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	Issue Date	Pages	Document ID	Title
1	20040513	163	US 20040091856 A1	DNA sequences from staphylococcus aureus bacteriophage 44AHJD that encode anti-microbial polypeptides
2	20030911	65	US 20030171563 A1	Regulators of bacterial virulence factor expression
3	20030313	24	US 20030049706 A1	Novel histidine kinase
4	20021226	158	US 20020197605 A1	Novel Polynucleotides
5	20020523	20	US 20020061572 A1	Histidine kinase
6	20020110	17	US 20020004214 A1	Method to detect modulators of histidine kinases
7	20041005	151	US 6800744 B1	Nucleic acid and amino acid sequences relating to Streptococcus pneumoniae for diagnostics and therapeutics
8	20031007	88	US 6630583 B1	Antibiotics and methods of using the same
9	20030624	243	US 6583275 B1	Nucleic acid sequences and expression system relating to Enterococcus faecium for diagnostics and therapeutics
10	20030415	18	US 6548281 B1	Histidine kinase
11	20021224	19	US 6498234 B1	Compounds
12	20020625	17	US 6410263 B1	Histidine kinase
13	20010807	22	US 6270992 B1	Histidine kinase of Staphylococcus aureus
14	20010529	18	US 6238885 B1	Histidine kinase

	Issue Date	Pages	Document ID	Title
15	20010227	16	US 6194174 B1	Histidine kinase, 636 HK, of staphylococcus aureus
16	20001003	19	US 6127147 A	Sensor histidine kinase of Staphylococcus Aureus
17	20000606	21	US 6071894 A	Sensor histidine kinase of Staphylococcus aureus

	Issue Date	Pages	Document ID	Title
1	20030313	24	US 20030049706 A1	Novel histidine kinase
2	20020523	20	US 20020061572 A1	Histidine kinase
3	20020110	17	US 20020004214 A1	Method to detect modulators of histidine kinases
4	20041005	151	US 6800744 B1	Nucleic acid and amino acid sequences relating to Streptococcus pneumoniae for diagnostics and therapeutics
5	20030624	243	US 6583275 B1	Nucleic acid sequences and expression system relating to Enterococcus faecium for diagnostics and therapeutics
6	20030415	18	US 6548281 B1	Histidine kinase
7	20021224	19	US 6498234 B1	Compounds
8	20020625	17	US 6410263 B1	Histidine kinase
9	20010807	22	US 6270992 B1	Histidine kinase of Staphylococcus aureus
10	20010529	18	US 6238885 B1	Histidine kinase
11	20001003	19	US 6127147 A	Sensor histidine kinase of Staphylococcus Aureus
12	20000606	21	US 6071894 A	Sensor histidine kinase of Staphylococcus aureus

	Issue Date	Pages	Document ID	Title
1	20030313	24	US 20030049706 A1	Novel histidine kinase
2	20020523	20	US 20020061572 A1	Histidine kinase
3	20020110	17	US 20020004214 A1	Method to detect modulators of histidine kinases
4	20030415	18	US 6548281 B1	Histidine kinase
5	20021224	19	US 6498234 B1	Compounds
6	20020625	17	US 6410263 B1	Histidine kinase
7	20010807	22	US 6270992 B1	Histidine kinase of Staphylococcus aureus
8	20010529	18	US 6238885 B1	Histidine kinase
9	20010227	16	US 6194174 B1	Histidine kinase, 636 HK, of staphylococcus aureus
10	20001003	19	US 6127147 A	Sensor histidine kinase of Staphylococcus Aureus
11	20000606	21	US 6071894 A	Sensor histidine kinase of Staphylococcus aureus

	L #	Hits	Search Text
1	L1	15510	staphylococcus adj aureus
2	L2	285	histidine adj kinase$2
3	L3	17	l1 same l2
4	L4	676298	clon$3 or express$3 or recombinant
5	L5	12	l3 same l4
6	L6	104716	WALLIS SHILLING MOONEY ZHONG JAWORSKI WANG THROUP
7	L7	11	l3 and l6